MEETING OF

ARMED FORCES EPIDEMIOLOGICAL BOARD

Dalymple Conference Room (1425)

The U.S. Army Medical Research Institute

Infectious Diseases

1425 Porter Street

Fort Detrick

Frederick, Maryland 21701

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TRANSCRIPT OF PROCEEDINGS

MAY 12, 2004

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Tri-State Reporters, Inc.
43 Summit Avenue
Hagerstown, Maryland 21740

FREDERICK, MARYLAND MAY 12, 2004

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8:00 A.M.

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PRESIDENT OSTROFF: Let's go ahead and get started. Why don't we start, I'll introduce Dr. Kilpatrick again who will function as the designated federal official. He is the Deputy Director of the Deployment Health Support.

DR. KILPATRICK: Thank you, Dr. Ostroff. As the acting designated federal official for the Armed Forces, Epidemiological Board, Federal Advisory Committee to the Secretary of Defense which serves as a scientific advisory body to the Secretary Defense and the Surgeons General of the military departments I hereby call this spring, 2004 meeting to order.

PRESIDENT OSTROFF: Thank you very much, and we have a new board member that's here

this morning, Dr. Sue Baker, and so what I'd like to do, if possible, if once again we could just go around the table and have folks introduce themselves and to make a few comments when we get to you.

(MEMBERS INTRODUCED THEMSELVES)

PRESIDENT OSTROFF: Let me turn it over to Dr. Gibson.

DR. GIBSON: (Administrative comments.)

PRESIDENT OSTROFF: The first of the presentations will be on the Vaccine Admission Program and our presenter is Lieutenant Colonel Harry Slife, who is the director of the Chemical and Biological Defense Program here at Fort Detrick. And, his briefing is in Tab 10 and thank you for being here this morning.

LIEUTENANT COLONEL SLIFE: Good morning. As introduced I'm Lieutenant Colonel Harry Slife and I'm currently serving as the

Director of the Medical, Chemical and Biological Defense Program here at Fort Detrick.

Our program is focused on the development of medical common interest to both chemical and biological. This morning I'm going to limit my comments to the biological efforts which is centered here in the building where we're seated at USAMRIID.

This is the agenda I'm going to follow this morning. I want to give you an overview of our program prior to getting to the interesting part of the presentation which takes place in this building you're going to have to bear with me and live with the administrative portion of my program that I live with day to day so I'll give you a brief overview of the program, the business side, the admin side, a little bit about product development, which you're going to hear a lot more about this afternoon from Colonel Berte. And, then we'll get into the meat of the presentation which

talks about the actual science and the current status of many of our programs.

And, then a portion of our program that we're very proud of and that is the relationship that we've had with other government organizations, the broad agency announcement that allows us to solicit work outside of the DoD and then finally a summary.

Our program is really threat based and requirements based and we take our marching orders from the services and from the DoD and from the intelligence agencies and where that translates into our research program is that those intelligence gathering agencies assess the level of threat of the various organisms and chemical agents that we need to be concerned about in a battlefield environment and then translate that into a series of requirements that are interpreted by the services and Department of Defense; various agencies in the Department of Defense that I'll talk about in a

moment.

And, then that enters into the cycle here where medical countermeasures this is the focus here of the medical research.

Physical countermeasures which are our peers at the RDE Com at Edgewood Aberdeen Proving Grounds are primarily focused on, though we do have a piece of this especially in the decontamination part, and, then finally in the education and training primarily our responsibility being the training of medical care givers.

So the way this translates that threat assessment, then translates into requirements and this is primarily handled by the Joint Requirements Office which then turns to the Joint Program Executive Office that is currently the Army's executive agent and determines whether or not there are commercial off the shelf alternatives to these threats.

If there are not, then we turn to

our R&D, S&T environment that is headed up by the Defense Threat Reduction agencies. And, the Defense Threat Reduction Agency then determines whether there needs to be any modification to occur in technology or whether a robust R&D effort needs to be initiated and that's where the laboratories come into play where this threat then turns into requirements which then turns into programs that are headed up by the Defense Threat Reduction Agency through us, the medical research and material command as well as the other service laboratories in academia through an extramural program. So that's how it translates from what we need to what we get.

The medical research and material command's mission is translated right on our crest and that is to protect and sustain. In the area of chemical and biological defense that means development and assessment of medical countermeasures to these lethal agents.

Our effort is primarily here in

the State of Maryland though there is a robust effort extramurally that is nationwide as well as the other DoD laboratories that are found throughout the country. But our lead efforts that are headed by my office here at Fort Detrick are USAMRIID where we are today that heads up our bio effort and that also has pieces that are down in Washington, D.C., at both the AFIP and the Walter Reed Institute or Research.

Our chemical program is primarily at APG and there's a reason for that being co-located with RDE Com on the non-med side and then our efforts there are at the Institute of Chemical Defense and at the Edgewood area Aberdeen Proving Grounds.

Our program is really product-oriented. I like to use the conveyor belt analogy and I want you to keep this in mind for the next couple of slides, because we're going to use it again. But the conveyor belt analogy means that we take something and we work it from

a basic S&T or R&D environment through a product acquisition process to finally get something into the hands of the warfighter and then beyond that for life cycle management.

So there's a conveyor belt, it's a timeline, we're not in the business of doing research for research sake. We are in the business of applied research, something we're going to paint green, we're going to put an NSN number on it, we're going to stick it in the pocket of a soldier and it's going to save his life. That's what we're in the business of doing. And, if you're not doing that when you come to work everyday at either RIID or ICB then you need to question where your efforts are. That's what we tell our researchers every morning.

So let's translate that conveyor belt analogy to a little bit more complex layout here and this is really the acquisition process for the Army and we translated that into the

acquisition of medical products and you're going to hear more about this from Colonel Berte because this is really the acquisition process, not just the S&T process. But you can see that now our conveyor belt is running left to right and over here in the tech phase we have discovery or hypothesis and that translates into applied research and then finally here along the center timeline you get these diamonds that indicate the milestones in acquisition. Acquisition milestone A is when we come out of that initial assessment or concept development and we're going to now look at focus efforts in a downsize group of candidates. Tests efficacy in animals and finally at a Milestone B decision we're going to make a decision as to whether or not this is going to be something that we're going to take to the advanced development and field. And, I want you to keep that Milestone B point in your mind, because when we get to some of the products that are on this conveyor belt

right now you'll see that many of them are right here at this milestone, just before or just after. And, that means that when we go to the next timeline, which is the exact same timeline I just showed you here across the top, but now what we do is we overlay the FDA requirements.

This is the level of complexity that our peers in the non-med side have yet to really appreciate. When you're buying an airplane or you're buying a battleship or you're bringing a new even chemical weapons detector to market you don't have to worry about anything below this point. But when you're talking about a drug or a test, a diagnostic test, something that's going to be used to either treat or assess a patient, then the FDA comes into play and the rules we play by is nothing goes in or on or is used to treat a soldier that is not FDA approved.

So all of these issues down here come into play and you see that point right

here, this Milestone B decision point of going to advanced development also coincide with those clinical trials.

So that's where a lot of our products are right now. And we'll talk about those specifically here in a minute.

Okay, so let's now talk about the medbio defense research program. The program is divided up into three primary areas, but I want to add a fourth here and that is genetically engineered threats. It's a small effort right now but it's growing. Our efforts are focused in bacteria, viruses and toxins. Those that are highlighted here in black are programs that are currently active. Those that are in green we do not have a program active right now, though these have been identified as potential threats and are on the threat list.

But several of these cross over into the infectious disease environment and are comrades in the infectious disease research

program are looking at specifically these three cholera, typhus and Shigellosis.

The level of effort varies in each one of these programs and that's primarily based on the perceived threat and what I talked about earlier in the program design by the resulting funding that follows along with that threat analysis and requirement.

This is the research taxonomy. You can see there are six primary efforts, three of which are bacteriology, virology and toxinology coincide with those pairings I touched on earlier. Here are the genetically engineered threat piece. We have a DARPA transition piece and this is a means by which very high risks with potentially payoff research has a way of entering into the process.

As I said we are not in the business of doing research for research sake and so that limits some of our investigators ability to be innovative because there's a lot of

pressure not to look at very high risk ventures.

This is a way in which very high risk work can be done outside the realm of the our more conveyor belt industrial laboratories and have a means of entering into the process.

So when one of these stems out of the DARPA research program and shows a lot of promise it can enter right into the mainstream, because we already have a very close relationship. In fact right now there are ten programs that have come out of the DARPA initiative that's more currently funded through our biodefense program.

Then we have a diagnostics area because if you don't have good diagnostics it's difficult to interpret what you're dealing with over here. So we've got get better on our diagnostics, we've got to more stats, more specific and we've got to be innovative and that's why there's a lot of work going on in new technology.

The program focus is in these four areas about the vaccine and therapeutic side is about evenly distributed with regards to the fiscal investment, about 20% of our program is located in each one of these. Our diagnostic area is a little more modest, that's about a 10% and the DARPA portion is about 16% and with quick addition you know that that doesn't add up to 100%, because there's another piece down here that's not shown and that piece is Congressional mandated programs and that makes up about 38% of the programs.

But you can see that there are efforts ongoing in every one of these. Obviously this is where the DoD would like to invest the majority of its time and effort. We want to have soldiers prepared before they go into a threat environment.

We don't want the logistical -- medical logistical burden and we don't want to lose the combat effectiveness of the soldier by

having him down here in this one. And, we don't want to be pulling all of our docs and all of our medical care givers to be dealing with those soldiers if we can protect them. So we really want our effort to be here and up here as well, because we've got to be able to determine what we're dealing with in order to make sure, so everything is related.

I mean, you can't be a good therapeutist without good diagnostics. And, we need to have good diagnostics in order to have good development.

A lot of challenges, that's why we're in business. I'm in control of everything. This is some of our products that are currently in the tech phase that are in the process of transitioning and I'm going to touch on each one of these in the rest of the briefing.

First the Anthrax vaccine and plague vaccine. Anthrax, there are two lead

candidates, one from the medical research and material man here at USAMRIID and the other is a British product. Both vaccine candidates have shown efficacy. At the Phase 1 trials for the MRMC candidate are just started. I was just notified of that that are starting at Vanderbilt and that process is being sponsored by NIAID. So that's good news. Both candidates are part of the NIAID long term strategy for stockpile for homeland defense. So you can see the work here at USAMRIID and you'll see this is a common theme throughout this briefing at the USAMRIID candidates are all lead candidates.

In the plague vaccine you see a very similar story. There are two candidates, one is MRMC USAMRIID candidate and one a British candidate. Both are based on the F1 and V antigenic determinants. But the difference being the MRMC candidate is a fusion protein whereas the Brit candidate is a cocktail of the two images.

Both have shown efficacy. We're currently at a Milestone A, the plague vaccine and MRMC plague vaccine reached Milestone A in January. Phase 1 trials will be based on a balance select between the two candidates.

Milestone B, the selection of the lead candidate is scheduled for Fy06.

For Venezuelan FY encephalitis vaccine, this is a recomminant vaccine that is based on site-directed mutagenesis of a live attenuated organism. This is the coding sequence and a series of site-directed mutations have been incorporated into the coding sequence to render it an attenuating virus and then it is cloned through an invitro process testing in animals and then ultimately in man. The current status is Milestone B is schedule for October of this year.

Phase 1 clinical trials are also planned. For toxins there are efforts going on in botulinum toxin, SEA and SEB and Ricin. The

botulinum toxin, as you know there are several sera types. The lead effort has been in sera types ending in B, though we have an ongoing work looking at C, E and F. The A and B product is reaching Milestone B in this year, FY04. There is no current vaccine for botulinum a licensed vaccine. Our researchers do have an I&E product that we use to protect researchers in the laboratory.

The staphylococcal inner toxin vaccine there again there is no licensed vaccine, but pilot lots have been made of the SEA. The plan is to do the same with the SEB and when the advanced development community and the requirements community feels that that has reached a level of threat that requires development that product is ready to go. But currently that is not funded in advanced development.

Ricin vaccine, again there is no licensed vaccine. Previous vaccine candidates

were chemically derived from the native ricin toxin and there were some significant manufacturing which is usually bad.

The current Ricin effort and candidate is made from the A chain and the A chain is mutated to render its (inaudible) inactive. And, that has shown to be efficacious in animals. And, it also this particular candidate, mutations may be met in that A chain has resulted in a product that is soluble and that was a big problem with the previous candidate. The mutations resulted in exposure of this hydrophobic part of the A chain that was normally massed by the B chain. And, that caused accumulation or aggregation of particles and particulates fell out of the vaccine. So this is a great step forward and we're looking forward to that milestone transition.

In the area of therapeutics obviously efforts in all three, bacterial, viral and toxin, the process here is to follow

classical developmental pyramid leading the FDA licensure. Efforts ongoing in each one of these areas focusing in immunotherapy and antibiotics and bacterial area a lead therapeutic effort in the viral area is smallpox and that is in -- use against smallpox and in the constant area the greater than 75% of the therapeutic effort of our program is focused on botulinum neurotoxins.

Medical diagnostics. The diagnostic areas really look in four primary focuses of the effort and that is assay development, identification of novel biological targets and then confirmation and validation of the technology.

In assay development we're looking at new improvements on old methods of detection. We have got to become much more sensitive with regard to looking for specific organisms and with regard to identification of novel biological targets we have to take advantage of the new tools that are now available in this

technology. Primarily use of bioschematics, use of in-vitro modeling systems and then taking advantage of molecular biology techniques, geneomix and proteomix.

Here again is the DARPA transition programs and I think I've already pretty much touched on this. Again, there are ten programs that are currently funded through our program and the objective is identifying the host promising approaches and focus on biological defense program objective. Like I said, this is need for those more high risk venture to find a means of venue for a tap into our mainstream program.

Shifting gears a little bit. Now, I want to look at the future trend. So those are the things that are right on the verge of transitioning to advanced development or have transitioned to advanced development. And, now I want to talk about the things that are back a little bit further on our conveyor belt analogy.

Back in the 6/1 research concept area of development and these are the areas I want to talk about. Genetically engineered threats, immunomodulator therapies. Multi-agent vaccines and alternative vaccine delivery strategies and early markers of infection first response. I won't really talk about these so much, but focus on the other four.

This is not something that has sprung just out of our program. Remember our program takes our direction from services and from the agencies within the DoD that identify what the threats are and what the requirements are. And, so there is a lot of evaluation that's going on in assessing where we need to be putting the limited resources that we have in the tech base.

So first let's talk about genetically engineered threats. The objective of this is to identify group, prioritize and assess the medical impact of non-traditional

toxins, various factors, genetically engineered microbes as biological war threat agents. I'm sure you can appreciate this is really a tough nut to crack, because how do you know where to start on something like this? Anything could be turned into a lethal agent, so where do you start your effort? What organism do you start with?

In the investigator series USAMRIID has taken a very logical and innovative way of approaching this issue and that is let's look at those determinants, those areas, those building blocks parts list for variants in various agents. And, then let's start a bioinformatic database, you know, of outside the lab let's do a lot of computer work before we go into the lab. And, let's assemble all of those things that we think are going to be used as a potential threat. What could people pull out of smallpox, for example, or pull out of plague that would no longer be in a vaccinia organism

but may be in something that would be a little more easily transmissible and yet still transmit the disease causing the portions of the organism.

So that's the approach that's been taken. It's more of a bioinformatic state right now where those kind of information are being assembled. It's amazing to me whenever I speak to the investigators that are associated with this as to how much information is available. If we could just get it altogether to assess exactly where -- what we should be looking for and then how to develop the diagnostics that are going to have to obviously follow in order to sort out what we're dealing with.

The concern that we all have is that we're always playing catch-up with regard to something like this when potentially what we could be doing is each agent that's released could result in a clock to start ticking in an eight year process to try to develop a vaccine.

Well, that's just not going to be acceptable, because by the time that we get around to a licensed FDA vaccine on the street we're already so far behind the eight ball with hundreds of these agents potentially be released in the interim. So we've got to develop a good way to assess what we're dealing with and how to deal with it with current therapeutic approaches and potentially prophylaxis that will have cross-over, you know, multiple agents.

Multi-agent vaccines, I can tell you I would much rather have something like this than something like this and this is the effort that is being pushed by the services. We want to reduce the shot burden, we want to reduce the logistical footprint on the battlefield where, you know, the classic medical guys that show up with their refrigerators and turn to the infantry guy and want to know where to plug it in in the middle of the desert. It ain't going to work. We're going to have to make sure that

we have reduced logistical footprint and a reduced burden on the soldier.

And, the primary efforts we're dealing with are the RNA replicons and the DNA vaccines, but you know obviously the feasibility's there. I mean talk to our veterinary friends, every animal vaccine is a cocktail and we already have, you know, in animal learning DPT as examples of mixed vaccines.

What we need to get an appreciation for though is that every single one of these vaccines prior to being mixed together or being used in combination like that have to be approved and then they have to be approved as a mix and show that there's not any metabolation of ethics to the vaccine because they've been mixed together.

So the path of licensure may take a while. But it's a good idea, it's always been a good idea. It's not limited to just the

military as being a good idea and it's an effort that's ongoing.

Alternative vaccine delivery methods. A lot of effort in this area, intranasal, transdermal, oral, other respiratory routes. It's another long range DoD objective. We would much rather be able to administer vaccines to soldiers in a more expeditious way than always having to use needles. And, there is a very robust S&T program that's working in collaboration with industry partners here and there are many of these efforts that -- a couple of them are highlighted here, transdermal and intranasal delivery means.

The recent flu vaccine I think, you know, is a good example of showing how efficacious the delivery can be.

Host responses to threat agents. In many cases, well, maybe not in many cases, but in certain cases organisms once they enter the body become masked or broken down or somehow

taken up intracellularly make it difficult through diagnostic means to identify what organism we're working with. The effort here is to take advantage of some of our genomic technology and proteo technology to look for specific response fingerprints once an organism is exposed to one of these lethal agents.

Do we generate a common fingerprint that can be used to sort what you've been exposed to. It's a very exciting effort, it's not only on the bio side but also on the chem side. In fact one of the investigators that used to work with me at the Institute of Chemical Defenses in the audience, Captain Medbelt, who headed up our genomics effort on the chem side.

Cooperation with Department of Health and Human Services. We're very proud of this effort. As you can see there's quite a list of programs in which we are working in concert with DHHS. Primarily NIH and so I don't

need to read this to you, but I think that this is a statement as to our interaction with those agencies that really helps us in a synergistic type of arrangement. The effort obviously in the civilian sector and homeland defense is in therapy, because it's not feasible unless you're dealing with a threat like smallpox. It's not feasible to inoculate, vaccinate the entire population of the United States. And, so a lot of the focus is on therapeutic efforts, whereas as I stated earlier the Department of Defense would much rather put our eggs in a prophylaxis basket because the longer we can keep a trigger puller on the front lines and not being pulled back through the medical evacuation process and burden the medical logistics training the better off we are.

We don't have enough soldiers to have every bed in every military facility filled. We need to have soldiers on the front line so we've got to protect them before they

get into combat, not after, so our efforts are focused on prophylaxis whereas our comrades in the civilian sector are rightfully so focused on therapeutics. You can see where there is a minimal redundancy there and a maximum synergy.

We're always going to have casualties and they're always going to have a segment of the population in the civilian sector that should be benefit from prophylaxis such as first responders. So there's a synergistic relationship there.

The broad agency announcement at the Medical Research and Material command is headed by our acquisition activity and this is a means for outside agencies to gain access to our research programs. This is the website and the reason I put this up here is because some of you may either be associated with this or may have some interest in submitting research proposals. This is a means to submit proposals that will be scientifically reviewed, ranked, ordered and

subsequently funded or specific areas for which solications are identified on the website. So if you are not familiar with that I invite you to take a look at that website and see what kind of efforts the program is looking for, because we're always looking for good ideas. You don't need to be a blue suiter or a green suiter in order to have a good idea. In fact the majority of the good ideas are coming out of the civilian sector. So we need to have a very close relationship, partnership in order for the program to move forward.

Finally, just in summary our DoD medical biological defense research program is a very robust program. I think it is a very healthy program and I think it's very a directed and focused program in the right areas. It is currently managed by the Defense Threat Production Agency, so the DoD program is not Army. All the services participate in our program as well as all of the federal

laboratories, academia and industry. You can find aspects of the program in every one of those sectors. It is a threat driven program so we take our marching orders from the services. They tell us what we should be working on and how much effort should be extended in each one of those areas.

The product candidates from pretreatment/prophylaxis, vaccine, therapeutics, and diagnostic research areas you can see that we're covering all the bases. It's not just focusing on vaccine. We realize that there's a therapeutic portion of this. We realize how critical the diagnostic piece is and so we have an investment in every one of those.

Then we have a very robust extramural effort and I think that the program greatly benefits from being able to reach out to the extramural community, especially the academic community and take advantage of the efforts being made.

So that's all I have and if you have any questions I'll be happy to try and answer them. I have the greatest job in the world, because I get to stand up here and tell you about all the great work that's going on, but I'm not in the lab doing it. So the folks that are here in this building are the experts. They are the ones that are really doing the hard work. And, then I get to stand up here and take the credit which is great. I wish I was a scientist.

COLONEL GIBSON: Thanks very much. You know, having been on the board now for a number of years we've had presentations and speaking for all the board we always get very impressed with the depth and quality of the research activities which are going on within DoD and this presentation I think was just as high quality as the other ones have been over the last couple of years. So congratulations I think it's a terrific activity and a terrific

effort and you and everyone else who's involved need to be commended for it.

PRESIDENT OSTROFF Before opening it up to questions from board members, let me just raise a couple questions for you that maybe you could address. In your list of what you're working on -- we made decisions about what you do intramurally versus extramurally and that the third quick one is, I didn't see any mention in your presentation of the homeland security activities in the S&T sector and I'm wondering whether or not there is what the impact, potential impact of the biodefense campus is going to be in terms of what your activities and your portfolio are?

LIEUTENANT COLONEL SLIFE: Okay, sir. Well, tularemia first and then there is an effort and it's modest and it's ongoing tularemia. As I said we're taking our marching orders from the DoD and from the services. Specifically, the Joint Requirements Office and

the Joint Program Executive Office.

Those two agencies really set the tone as to where our efforts are going to be. Tularemia has not been determined to be a high level threat in the context of the other agents that we're working on. With the limitation on the resources that are available Tularemia has been relegated to a lower status on the threat list. That does not mean that it is not considered to be a threat, but it certainly does not mean that we would not entertain any suggested working that area.

But it would be a case by case basis and that kind of leads me to your next question, sir, which is the process by which we determine where we put our efforts. Specifically in the case that you mentioned, intramural versus extramural.

What we've tried to do is break down barriers there between intramural and extramural programs in that especially now that

we've transitioned the management of the program from here at Fort Detrick in my office down to the defense threat production agency, specifically the chem bio cell. And, what they're doing is they have what they call capability area program office and each one of those areas focuses on a specific portion of the program; one is therapeutic, one is prophylaxis, one is diagnostics and one is special projects such as non-traditional agents.

Now, each one of those areas has assembled from academia industry, DoD, a panel with which they call their scientific review groups in which they are reviewing all solicitations for alternate rank ordering within the priority of the program. These capability area managers are setting the priority based on input from the Joint Requirements Office and the Joint Program Executive Office as to where they want to put the focus of their effort. They are looking at both extramural and intramural

solicitations.

Many of the extramural programs that we fund are multi-year and so they somewhat have an inside track, because we certainly do not want to make a sizable investment in one of our academic partners and then cut them off after ten or twelve months of effort. And, so those are sort of at the top of the stack and the benefit to program and current status, the progress that has been made since the contract has been awarded are all evaluated as to whether or not that contract ought to be continued.

But what we're trying to do is break down the barrier between the intramural and extramural program so that what we're doing is we're buying the best science for the warfighter and we're not worried whether that's done at Vanderbilt or whether it's done at the University of Maryland or whether it's done at USAMRIID.

Now, certainly we have a couple

other issues we've got to concern ourselves with and that is USAMRIID can use agents. They have the L4 ability, they have the bio -- program. Similar to the Institute of Chemical Defense they can use live agents there, meet nerve agents in their facility.

There's a lot of places in the United States that -- I mean the majority places in the United States you can't do that. You can do simulation up to a point, but at some point when you're dealing with these kinds of agents, chemical and bio you have to use the agent that it's concerned with and you have to go in with the animals and do those.

And, so those things have to be considered. We can fund work extramurally to a point. I don't think that there will ever be a time unless we can go BL4 level all over the country where facilities as valuable as USAMRIID or the Institute of Chemical Defense will no longer be needed. That is such a critical piece

to our program and there's not a lot of places that can do that.

With regard to your last question of Homeland Defense, our program has not been actively engaged in that, but certainly we are looking forward to the ANTH (inaudible) and that synergistic relationship that will exist right here at the Fort Detrick campus.

I think that that would be a great boom to our program, because as I said with our relationship with DHSS right now and to some extent I think we can greatly benefit from each other's experience. Right here at the USAMRIID there are investigators that are recognized internationally as the expert in their particular areas.

And, to be on campus with someone like that that you could actually go over and have a cup of coffee with and talk to them about something I think it would be a great benefit to both of those teams. So I look forward to that.

I'm not sure how the program is going to evolve once the impact becomes a reality, but I'm looking forward to it because I think that certainly it's going to be a benefit, it's not going to be a determent to our program.

MR. HERBOLD: John Herbold, my question is about the VEE vaccine development. Can you tell me two things, how does the efficacy of this new vaccine compare to the one that was pulled out of the stockpiles in the early '70's to deal with the episodic...

LIEUTENANT COLONEL SLIFE: Okay, sir, I cannot tell you the efficacy differences on that. What I can tell you is the information that was passed on to me, because I'm certainly not an expert in vaccine development nor in equine encephalitis. What I can tell you is, is that the investigators that have been working on this vaccine are actually very excited about it and the fact that it has shown great efficacy I certainly would think that this is a step

forward.

We certainly would not be looking at going to Milestone B with a product that was less efficacious than a product that was already licensed.

MR. HERBOLD: My followup question also is it seems that a multi-male encephalitis vaccine might be something that would be worthwhile to pursue, both in...

LIEUTENANT COLONEL SLIFE: Yes, sir...

MR. HERBOLD: ...context and also in the environmental exposure -- has that been considered because there are a lots of...

LIEUTENANT COLONEL SLIFE: And in fact..

MR. HERBOLD: Has that been considered because there are lots of...

LIEUTENANT COLONEL SLIFER: Yes, sir. And, the recommitant vaccine that I spoke of is being pursued on that track. And, in

fact, has shown efficacy with at least I believe three other sera types of encephalitis. There are tests that are ongoing between Eastern and Western as well (inaudible) and so far as good. I mean the results are very promising that there is crossover evidence...

DR. GRAY: Very interesting, Colonel, thanks so much. You mentioned a new bioinformatics effort. I just wondered how that might be made from the very remarkable effort that's involved at the NIH with entree and blast and all those things. Why do you need a supplemental bioformatics?

LIEUTENANT COLONEL SLIFER: I certainly don't want to give you the impression that we're developing something, you know, (inaudible) we're, not working in a vacuum here. The lead investigator here, Lieutenant Colonel Charles Mallard, has really taken into consideration all of the existing capabilities that are out there and are pulling them

altogether. All I meant by stating that we were developing bioinformatic cell to tap into in this genetically engineered threat environment was that we were just taking advantage of the current capabilities that were out. We weren't developing a new database. Certainly weren't trying to replicate something like NCPI or the blast capability that exists out there. It's just a matter of tapping into those and being able to bring all of those points of life together in order to give us a subset of information that we need in order to move forward in this genetical engineered threat.

COLONEL PULLIN: About four years ago or so I was on an island that looked at how things were prioritized and then going from a tech base to advance developing state and he identified a number of significant factors that together sort of conspired to present the sort of progress that apparently is now happening.

So my question is there were

problems identified with agencies not sort of being lined with one another. Difficulties in securing all kind of funding which you talked about briefly. And, difficulties in moving particularly from the 6-1 to the 6-4 stage phase have changed in four years. Have they significantly changed and advanced your ability to sort of follow this conveyor belt?

LIEUTENANT COLONEL SLIFE: Well, I believe they have. My involvement at that point in time was down in Texas and I can tell you there was a lot of frustration in feeling that there was a lot of effort that was being put forth in the tech base. It was not being translated into something that soldiers use. And, I think that has really changed and I think that you're going to hear a lot about that in a few minutes from Colonel Berte, because primarily due to the efforts of these other agencies that I talked to about the JRO and the JPEO and CBMS and chem biomedical systems they

recognize that there needs to be a technology pool from the fielding and deployment environment as well as the technology push from the tech fields and obviously the ratio should always be greater than one to one for tech base through advanced development.

We always want to be developing more than the advance developer can take. That way they can be very selective about what they take and they take only the best and put their resources to the best use. So there's always going to be some of that level of frustration from the tech base that our stuff is just not getting out to the field. But that's because they're doing their job and they're focusing their efforts.

So I think that it's a good thing and I think that your assessment is right on the mark. I think that we are doing a better job now than we did four years ago or even a couple years ago. I think the rules have been laid and

the Army, specifically, I think all of the services, but I can speak for the Army because I'm a green suiter, there is a lot of focus on acquisition training now. We never did that before. The Army Medical Department never played by those rules. And, now every one of us is required to go through extensive acquisition training so that we can sit down at the table with our non-medical comrades and we can talk the same language and we know what milestones they are. Milestone B and advanced development and life cycle management and all those kind of terms that we never spoke of those before. We had no idea what those were.

I think that that's really where the effort is in acquisition training.

MR. PARKINSON: Thanks, Colonel Slife. Mike Parkinson. (inaudible) summarize about forty percent of your budget has mandated programs. Can you give us an idea of the major topic of those programs, also just the sense of

the trend of that budget proportion over time, the last five years or so and then finally what's your professional Intel tells you what's on the pipeline currently on the Hill for what I think was a growing proportion of the budget.

The second question is in a general sense is as I look at the systematic approach to the threat, you know, development time lines, conveyor belt, we thought yesterday really getting a true threat assessment and again we're all from scientific medical backgrounds. We love vaccines and toxins and love antibiotics but the real threat assessments today is people being pulled out of (inaudible) have you ever thought of the application of this model, product development concept, for a behavioral threat assessment and use a similar industrial approach addressing the problem? I know it's not your responsibility, but I wonder if this board -- it would seem to me that we never tried to apply this. But it might not fit

exactly, but maybe there's something to get us off the -- like compliance and things like that. We just aren't making any progress. There are things we have to approve in the actual application...

LIEUTENANT COLONEL SLIFE: Well, in answer to your question with regard to the Congressional mandated programs that is an area obviously we have no control over. I think that -- I've heard a lot of criticism of that program, but I can tell you that from being inside where we have to actual manage those dollars, there's a lot of thought that goes on before those programs are awarded and they are not just work handout gifts to constituents. There is a lot of thought put into who gets those awards and a lot of them are ongoing efforts that have been funded over several years.

I know the University of Michigan, for example, one that I'm most familiar with is

doing a great effort in the use of lipizones as a delivery needs for therapy on mustard agents and so you can see this isn't something that somebody's doing hobby science and getting the Congressional constituents to give them a bunch of money to do it. This is a peer reviewed scientific efforts that are in line with the program and may be for whatever reason are not coming through other mechanisms to gain funding such as the broad agency...

That's really all I can say about that issue, because that's my level of involvement.

I don't know where the program is going. You know, certainly I don't think it's getting any smaller. But so long as it is in line with our program objectives anyway it's fine with me and certainly I don't have any say on whether it's okay or not. We execute that program and it's a good one, it really is a good program.

With regard to the behavioral assessment I agree with you, but again that's pretty much out of my area of control. But I think that this same kind of acquisition analogy could be used across the board and is being used. Maybe not so much in behavioral, but certainly in the non-medical acquisition process. We adopted this from our big Army brethren that's what they use to, you know, to develop fighter aircraft and to develop the next battleships.

But, you know, that's the same acquisition process, we're just applying it in the medical environment and so we're facing a learning curve what our Army brethren have been doing for years. We're just now applying it in the medical sector.

DR. PATRICK: Again, it's a very impressive presentation, but what I'm impressed with is just how big this area of research is becoming. I note on both the Anthrax and Plague

that you're also looking at some products (inaudible) UK. I'm wondering in what way is this research agenda planned to be coordinated potentially with other countries, because in many respects the problems (audience noise) potentially in these (audience noise) American business are everywhere now. This just seems like it's getting to be too big for us to manage on our own.

LIEUTENANT COLONEL SLIFE: Yes, sir, we are -- all of the problems that I brought up, all of the issues that we're addressing here are not limited to the borders of the United States and all of our allies have similar type efforts and it's ridiculous for us not to take advantage of their work as they take advantage of our work. There are many international agreements. Most notedly is what we refer to as the (inaudible) agreement which is, (inaudible) in which we deal both on a classified and unclassified setting with all of

these agencies and we readily interact with them. We share information and we also divvy up who's going to do what so we're not doing a lot of redundant efforts and redundant spending.

The Canadians have a great research effort going on out in (inaudible) and the UK has a (inaudible) facility that has some of the international and renounds experts in all of these areas working primarily on the chem side, but also efforts in bio side. And, the T&L laboratory in the Netherlands is another one that we deal with on a regular basis. Our researchers are on first name basis with those folks. We interact with them routinely.

It is not an exception, it's the rule that we interact with our international brethren and obviously our closer allies we have closer contacts with there are efforts ongoing with Israel and as I said Canada and the UK and the US have a very close in international agreement in which we meet routinely and try to

eliminate any of those redundant efforts and identify what threats we're all working on.

PRESIDENT OSTROFF: Thanks so much. You've been up there for an hour and we really appreciate you taking the time out of your schedule to brief us on this and we continue to be very impressed with the effort.

(Short recess taken)

(Colonel Gipson gives announcement)

Now, we're going to hear the presentations on the acquisition side of the world. The presentation on research and our speaker for this session is Colonel Stephen Berte who is the joint project manager of the chemical biological medical systems and he's going to give us a status review of chembio acquisition after DoD.

COLONEL BERTE: Thank you, sir. It's a pleasure to be here to talk to you about acquisition and give you an update on where the DoD acquisition program is from medical records.

This is an agenda to give you an idea what we'll be talking about, a little bit about organization and some changes that have occurred through the last year. I'll talk about some challenges and then talk about two of the programs that I manage.

April 2003 the chem/bio implementation plan was put into effect. This was a congressionally mandated reorganization of the DoD chem/bio defense program which mandated that all chem/bio defense products including medical all be rolled up into one coherent program. So it falls under the defense acquisition executive who's currently Mr. Lynn, Michael Lynn. The Army acquisition executive reports to him. The Army is the executive agent for the program and that is Mr. Clyde Bolton. And, then the joint program executive officer or chem/bio defense is responsible for advanced development. And, that is General Steve Reeves.

And, then he has to be in seven

project managers, in which I am one, that chem/bio defense program medical and non-medical. All medical items, medical in terms of FDA type issues fall under my purview.

When the implementation plan was put into effect it included three legs of requirements that are determined by joint requirements office. The science and technology is handled through the defense threat reduction agency, chem/bio defense directorate, which we've heard some discussion about I've heard in the last discussion.

Then advanced development is handled through the joint program executive office. It's sort of a triad of requirement, tech base and advanced development work together to run the program.

The way chem/bio defense program is run is that it is a system of systems so that the medical products are integrated for a pre-treatment, of course vaccines and we have

treatments autoinjectors and the like and they are integrated with all of the other counter measures that are available for the troops including suits and masks and such.

I stress again that the medical side that we handle does not include things like medical shelters and any kind of medical device that might be in the chem/bio defense arena that does not require FDA approvals does not -- we don't have that. That would be collective protection handles the hospital sets for bio/chem defense.

So we have General Reeves here and I said there's seven project managers under him. I am one of the chemical biological medical systems. Beneath this command level there are two additional commands. These are at the lieutenant colonel level. The joint vaccine acquisition program is commanded now by Lieutenant Colonel Travis Ber... (inaudible.) And the medical identification and treatment

systems is currently -- the product manager there is Lieutenant Colonel Ed Claysen.

So many of you are familiar perhaps with JVAP, but until the implementation plan came about that was kind of the need for vaccine development, but when the implementation plan came along and incorporated all chem/bio defense assets under one umbrella, that pulled in the chemical side and so the mix was born. So these two commands I support both of those commands.

So that's our mission medical, protection and treatment capabilities.

The challenges, the FDA laws, this may seem like a blinding flash of the obvious to many in this room, but it's not that obvious to a lot of people even within the government that they say, often they say "you're DoD, why do you have to follow all these regulations?" Well, as we all know soldiers, sailors, airmen and marines are U.S. Citizens too and of course the

FDA's, purview is to make sure that anything we put into U.S. Citizens or anyone in the United States is safe. And, so all the FDA laws apply and really do drive our program.

So we're within the acquisition system and within an acquisition system you have to have test and evaluation master plans or temps for a weapons system and my shortcut answer to that is in our program we spell attempt FDA, so we don't have a separate -- and the system allows for that. There are regulations which I've stated straight up that you don't have to have an temp for vaccine as long as it's FDA approved it meets all the gates that is the intent of ... So FDA meet prioritized warfighter needs within available resources.

Again that may seem like of course you have to it within resources, but how they do that I'll touch on a little bit later. It's changed a little bit to make us I think a little

more efficient.

And, then of course we have the challenge within the FDA guidelines of proving efficacy of chem/bio defense medical products. Of course now we've got the animal rule so that makes it a little bit easier; not necessarily cheaper or faster, but at least we can get there from here which of course before 2002 when the FDA rule, when the animal rule was put into effect we couldn't do, since it's obviously unethical to be testing people with live agents.

So first we'll talk about JVAP vaccine development. Here's a little history for you to kind of put things in perspective. If you look at the DoD as a whole and consider it as kind of a black hole that's out there. One could say we have been criticized for not getting things out the door. There are a number of reasons for that. One, I think you can see from the funding line this is advanced development funding. You can see the lows are

pretty low.

Chemical program they have remained fairly low although they are starting to increase. For the vaccine program they started increasing in 1997 and actually in '97 is when JVAP was established and that was coincident with the beginning of an increase in funding for vaccine development, but it wasn't until '98 that the prime systems contract was put in place. So JVAP was established, it was effective by '98 and it had the vehicle to move forward in development programs.

So vaccine company, BBC is our prime system contractor for the vaccine development. And, so as the funding line has gone up we've been able to move things forward. It wasn't until out here in '02 when the Animal Rule was put into effect. Shortly after that there (inaudible) was approved under the Animal Rule and to date I think it's still the only FDA approved product that's been approved under the

Animal Rule.

Now, if you look at industry standards the clinical trial phase that is from IMB submission to the DLA submission is roughly is six plus years on average. Some are less, some take a little more. So taking that industry standard that's what we are trying to achieve. In fact we will have -- so you have an increase in funding. You know go back to the Gulf War and say, what have you done since the Gulf War, well, we had some limited resources, resourcing started coming up in '98, you take '98 it's kind of a start date when funding increased and then along the way we also got some help from the Animal Rule.

Our first product coming out will be the approval of the licensure of (inaudible) globulin -- will be out in '05.

And, as we dub other programs we're gearing for this industry standard average to get things out. So from the time JVAP was

established until the time it's starting to pump things out we feel we're kind of on schedule and we're doing everything we can in terms of funding and dealing with our funding to keep those schedules as short as possible to get them out in industry standard time.

Acquisition strategy. Again addresses user requirements based on Chairman of the Joint Chiefs. FDA licensure is what we're after and we're not interested in stopping at continuancy protocols. Though we see that as a way point along the way. Particularly we see this is a way that we can working at the interagency as well leveraging bio -- funding in that we can take things, get through Phase 1. Phase 1 is sufficient whether we do it all at once or in Phase 1A and B, if you will, get to a contingency protocol status. At that point we should be able to leverage -- funds to put some material in the stockpile that could be used under emergency situations.

Now, we would then continue forward with licensure to make sure we're getting them. In the interim if something happened, if some challenge faced the nation we can at least have something that we can pull off the shelf and use. But licensure is our goal no matter what.

Leverage international partnerships, other government agencies, I've heard you talking about that. Again (inaudible) chem/bio radiological (inaudible) Canada and UK and US. We have a project arrangement now for smallpox vaccine system under that.

Now, DoD the smallpox vaccine program was terminated, the vaccine portion. Though the VIG IV's continuing forward.

However, these things are kind of linked because what we're doing is relooking our program and coordinating with other agencies like Health & Human Services to make sure that we're not doing redundant systems.

So the fact that we don't have a smallpox vaccine program we don't see as a problem, because of course DHHS and in working with right now a Canvas (sic) is moving forward with their own vaccine.

Of course there's a hold placed on that project, we don't anticipate, as I am sure many of you are aware, it's not surprising that they found some adverse reactions given how carefully they were looking for those adverse events within the smallpox vaccination trials.

So we believe that will go forward and that would be an option for DoD to purchase that product once it's licensed. So that has been running two parallel programs so close to coming to fruition at the same time will leverage their efforts. We can do that in other programs as well.

But the idea of these project arrangements in this case with Canada is that we achieve -- get around the problem of no

harmonization between the regulatory agents of various nations. Harmonization, of course, has been an idea and I don't think anybody in this room is going to live to see it.

So the way to get around that is to co-develop products and make sure that when we license it in one country it's licensed in -- well, in this case it's just Canada and the US, with smallpox. But it's licensed in both countries, so there's a certain amount of inoperability there between the forces and if they are using the same product the product is licensed in both countries.

We are negotiating a project arrangement with Canada, UK and US, all three countries under the CBR-MOU for a plague vaccine. That is still in the -- process and currently working it's way through the system.

Again, the concept being that at the end we end up with a plague vaccine licensed in all three countries. The way that works is

that there is a cost-sharing incorporated into the plan and the cost-sharing occurs on all joint -- on all equally applicable items.

For example, there's clinical trial, all three countries need clinical trial, so all three countries share. When we get down to things that only one country needs then that country pays a hundred percent. The obvious things would be at the end of some of the regulatory things that need to be done.

So anything that we all have to do to share costs and anything that is unique to that country pays for it, in the end then we end up with a plague vaccine license in Canada, UK and the US, would be essentially the same product.

I mentioned this already, we're trying to manage our funds to make sure we get things out to minimize schedules. And, the way we'll do that is we're going to expand or contract our product lines. In the past we

haven't always done that. We have salami sliced our budget where we've had multiple programs running because the programs were ready to come forward. So the tech base does great work. The standard for vaccines is key player obviously, they're a very important player. They make these products and have them ready for advanced development and in the past often we would take them if they were ready rather than saying, "but do we have the money to do it."

Well, we have the money and we could take it from other programs, but what that does, of course, is stretch your product development time. What we've said now is we're refocusing. We're saying we're using the priority list. We've prioritized the products, we're going to take all the money we think we need to get it out in industry standard time and if that ends up with one vaccine or two or three so be it. But we're not going to take any more. So if something comes down the pike and it's

ready to go to advanced development, but we don't have the money for it, then we're not going to start it. It's going to have to be developed in some other way. It won't come through us, because we just don't have the budget to do it and we won't slow down other products to do that.

But thinking back to all the players here we do coordinate with the tech base through DITRA and directing with the tech base to determine what's coming down the road so for example we're in the midst of (inaudible) right now. Looking at the '06 to '11 years and we have feedback on what we anticipate coming down the pike for advanced development and when it's going to come and we put in requirements, unfunded requirements at this point, in the (inaudible) to try and get money to support those products when they do come down. So we are coordinating.

We have a vision of where things

are in the system so that we get a linkage between the tech base and advance development in terms of funding so that we don't have to say, "stop right there, we don't have the money to do it."

There is an advanced planning process underway which seeks to infuse money into the chem-bio defense program, not just the medical program. We do have a list of UFRA's submitted so that if that money comes through, our UFRA list to tell you that we're trying to do as much as we can based on what we see coming down the road is Half a Billion Dollars that we put in. How much of that is going to be funded I don't know, but we have visibility of what's coming down and we're requesting funding for this high priority -- and trying to get as much developed as we can.

We won't know what the result of that is for some time, but I think you need to have a feeling that we are looking to see what's

coming forward. We've got a plan in place, we've got a prioritized system and when we do get a product we want to move it forward.

As I said FDA drives cost schedule performance and we were touching on this in the last DoD 5000, that's the acquisition regulations. The new one particularly that's been done in the past few years updated for the past couple years is definitely tailored and adjustments can and are made to accommodate the FDA problems. We don't see a problem in bringing products forward within the acquisition system, because it is sufficiently flexible and we can get there from here.

There are medical corollaries to the DoD of 5000 technology readiness levels, the weapons system near levels are used to assess the technology to determine if it's ready for prime time, so to speak, at any given point. It's ready to go to the next step. And, MRNC has and subsequently has helped in fine tuning

the TRL's and has made medical corollary students speak in terms of FDA processes and how that fits in the system. So, that's part of the documentation that's out there, the acquisition system looks at it and sees and understands that it's ready for acquisition.

Evolutionary acquisition is something that we use when possible. Of course it's difficult since it's, you know, technology insertions is kind of tough under the FDA process. Once you enter the clinical trials and you make a change to the product then obviously you have to go back and restart, so it's a little difficult, but whenever possible we'll look to doing these sorts of things. I wouldn't say at all that there's any kind of inordinate pressure. This is kind of a buzz word within the acquisition system. You have to do things in an evolutionary fashion to kind of build on what you have and insert technology as it comes out rather than just plodding along with one

product and then by the time it comes out it's behind the times.

Those things don't quite apply to these medical systems and the acquisition system. The DoD acquisition system I think understands that. So there's no undue pressure to do those sorts of things.

The unique thing, because of the inability to get the technology inserted is that we need to have -- we need to work within the system to get our requirements defined a little bit earlier.

What we don't want to do is to get down to Milestone B and that is -- that's the official program initiation for advanced development.

We don't want to wait until that time to find out the parameters that are going to be placed on the product can't be achieved, because by the time we get to Milestone B we're already moving down the road to clinical trial

so the product is pretty much defined by that point.

Again, a challenge, but not an obstacle in terms of working within the DoD system.

What this does, just to give you a quick -- you'll be able to read everything, it's more of a concept slide here is it's showing that integration of the regulatory and acquisition process is here you can see the -- what this shows is the manufacturing steps, for example, in green and blue steps are testing here's Phase 1 human, Phase 2 expanded safety. Things out here, animal efficacy is in there. This is assay development. So you've got your FDA process and what we've done is overlay that with the acquisition process. So you see Milestone A here is proof of concept in your animal studies roughly is when you enter Milestone A and Milestone B occurs after you've had Phase 1 successful Phase 1 clinical trials

in general.

That's the acquisition process. Milestone C and you're getting into production and deployment is right about the time shortly after that is when you'll be submitting your BLA submission.

So you can overlay the FDA process with the acquisition process and it works fine. You can fluctuate around and it's not an obstacle. It was more difficult in the past I think because the acquisition system (inaudible) but that's no longer the case.

I touched on this already a little bit. What the industry trends are. Just to give you an idea of some of the products that we have out there now being developed are scheduled for botulism vaccine. This is the AB -- recommitant AB and plague vaccine, so again we're funding things to get them out in the appropriate amount of time. And, advanced anticonvulsant system is a little longer.

That's due in part, because we've passed some gates where we could have shortened it and we didn't have the funding at the time. As funding increase that we did get ruled out in the future. That is definitely our focus.

We're always looking for ways to shorten the schedules. And to get capability out there and I think as the bioshield moves forward, at least get the capability out there and move forward down the road to licensure.

Some of the interagency challenges is sometimes a difference in emphasis. This in part is due to the populations that we support. DoD has a small population of sick adults who go in harm's way routinely. So prevention is the emphasis. Our Health & Human Services and Homeland Security treatment tends to be more of the emphasis, because you've got a much larger population vaccinations everyone in the nation is not the preferred method, rather depending on what it is. In some cases it may be, but

treatment is a lot more -- is more heavily emphasized. Again, this isn't black and white but it's a general trend.

I have already touched on this. So we're leveraging DHHS efforts but we have to make sure that they are focused on licensure and that they meet warfighter requirements, because we want to have licensed products. We're not interested in stopping at the contingency protocol stage. And, we need to meet our requirements, which may or may not always mesh exactly.

We are seeing significant gaps between our programs. There is some overlap in some complementary programs and just as a quick view, if you look in -- and these X's mean either tech based or advanced development, these are things that DoD is interested.

Of course there's a lot of overlap between what DoD is interested in and CBC category for example as you can tell by looking

at this.

Here where you see advanced development this means we see things coming out of the DoD tech base into advanced development in these years and we have plans to deal with that.

Anthrax, of course we have AVA on hand and available now. DHHS is developing follow-on and somewhere down the road we may decide to switch or not. It depends on what the end product looks like. I can tell you what we are planning on doing is looking at a briefing study so that in the event DoD decides the new product is better and there's funding out there that we can find out, can we use a new product, for example, to those people who are in the midst of this program so that we can get some continuity and not have to have two different vaccines entered into the system.

So we are putting plans in place to allow for that contingency, but it's too

early to say what is going to happen We're working with DHHS on this program in that we essentially have the lead for developing the AD. We've had meetings with NIAD last week looking at can we incorporate the E (inaudible) type into this Thrivalin (sic.) We're looking at that. The concern is how much it's going to slow down the AV project. What we don't want to do is say, "yeah, this is great," but then have to wait three or four years to have any kind of product. If that's the case then we'll say we need to continue moving forward with AV, for example, and then we'll look later into having an -- either taking -- perhaps one option might be to get AV license, get E license and then come back and look at studies are putting them together some how.

But we are working closely with them on that. So (inaudible) working with international in an interagency fashion.

Right now the AVA's in production.

These are programs that are currently funded up here. Now, we're also working on V, and a caveat here you see the line in the present time and the reason that is, is that it's in the DoD unfunded program is that we have funding through this year, but from there out we don't have funding. But we have put in a UFRA (sic) to get this thing funded. I'm optimistic that it will continue. And, so what you see then is licensure dates the stars are to anticipate licensure.

So they will be out in '05 and Bi A/B plague we anticipate they will be able to continue forward and then what we see coming down the road in the near term is Ricin and SE. DHHS programs, of course, they're got their smallpox, they also have a big product moving forward. I think that ongoing -- tularemia is the product that they have is a DoD product that we've transferred over to them to get to Phase 1 trial done. So they're working now, to my

knowledge there's no transfer of licensure of that product at this time.

BOT CEF, DHHS is interested in all seven sera types. The reason I just put CEF in that is because the DoD requirement is for ultimately focus on (inaudible) so that is why we mention CEF. So there is ongoing work going on in DHHS as well as DoD with no definite plan as to when it is going to get out.

Shifting gears quickly to medical identification and treatment systems. These are the drugs and creams and devices that meet FDA requirements. Just to give you a quick list of things that have been FDA approved. Now, this program recently shifted over to the chem/bio defense program. Initially it was tech based. The tech base in advance development and it shifted over to the -- the advance development shifted over to CVNS. But many of the faces of the people that were associated with the advance development of these products are matrixed over,

a lot of people from USAMRIID are matrixed over to CVNS to manage these products. The deputy is Ron Claussen.

So the autoinjectors SERPACWA. You know we get beat up a lot in the military on acronyms but I just want to give credit where credit's due and FDA is responsible for these.

We wanted this to be TSP, topical skin protectorate, kind of told you what it was doing, but I have to be fair to FDA, FDA didn't say, "you have to call it SERPACWA." They said, "When you name this it ought to have words in the title of what the product is like, that it's a skin exposure, it's a paste that reduces skin exposure and it's protective against chemical warfare agents. We'd like to see all those words in the title." So pretty much when you get there that's how you end up with SERPACWA.

So, these are some of the products that are out there with FDA approvals. But these are some ongoing products. Advanced

anticonvulsant system replaces diazepam with midazolam. Next generation oxime or the improved nerve agent treatment system. This is replacing with the new oxime ingredient which is still in the process of down selecting. Doing some final testing on down selection and the idea is to have something more effective against the non-traditional agents. As part of this we'd also like to do some studies to expand the period of (inaudible) SNAPP the majority of tests was done with SOMAN (sic) as a representative nerve agents. What FDA said is that we really want to see -- if you want indications for other things you've got to do more testing with those other agents before we're going to make it a broad indication for agents.

Bioscavenger, and specifically what we're focusing on in terms of protomatics is the recombinant butyrylcholinesterase. We see that coming down here in a couple years.

Again, all these products coming out, as with the vaccines, are big driver is the tech base within (inaudible) and it's coming out of ICV.

Now, we also have diagnostics now. And this is an example, if you will, of evolutionary approach in that it's going to start out as a detector and eventually become a diagnosing device.

So it's going to be fielded as a detector, but as we are getting it ready for fielding as a detector we are working with the FDA to start getting prepared to be converted over to diagnostic.

And, then the other program I have is the critical reagents program which a large part of that is actually non-applicable and that is providing all the reagents and assays for the entire DoD chem/bio defense program. So all the devices that are out there deployed with trooper that are in vehicles and all the detectors that

are out there that DoD uses these folks are acute player in providing and procuring and fielding the reagents that's support...

Just a little bit more on the JVAP based on the rapid system PCR system. It's going to have a short turnaround time and the idea is to have it deployed, it's got to be under forty pounds and we're there now.

So initially it will be fielded at ten assays. The next step you add six toxins and issue to the assays for various bioagents and then ultimately what we're shooting for is FDA approval as well as miniature so that eventually it is a hand held, that is the ultimate goal.

Here's a quick look at MITS products. Things that are in production now that are funded and unfunded we also have for the first time -- radiological, we haven't had radiological products before. The product that is coming forward is called the radio protective

and we are trying to get money in the palm to take that theory to '06 time frame.

These are just some JBAIDS Block 1, that's the initial ten assays, JBAIDS Block 2 is the (inaudible) toxin.

Block 3, this is unfunded as is Block 3 at this point where it began to work toward those programs.

So this is just kind of a review of what the DoD med chem/bio achievements have been. Again this is a joint effort certainly between USAMRMC as well as CDMS. MSAMRMC obviously continuously supporting on both the med chem and bio side from a tech base and before chem advance development of just last year so it's truly been a joint effort and the tech base is still obviously a fine (inaudible) we've seen things that DoD as a whole through joint and team effort has put out.

Between DoD, DHHS and DHS we've supplied strategic national stockpiling of

Anthrax. (inaudible)

Okay, with that I'll come to a close and I'll take any questions that you have. It's been a pleasure to talk to you. I've wanted to give you an idea, those of you who remember JVAP to realize we've worked quite a bit on the implementation plan to accomplish a lot more than just JVAP. JVAP obviously is still very important, but we've also got this chem side now that is of equal importance. Thank you very much for your time.

(APPLAUSE)

DR. KILPATRICK: Colonel Berte, thanks very much and thanks for your sharing the information with us. Let me open it up with questions before I ask mine. First Dr. Shamoo and then Dr. Shanahan.

DR. SHAMOO: Dr. Shamoo. The ultimate test for most of these agents and their treatment, the vaccine is going to be when the human beings are affected. Nevertheless through

bioshield you have contingency treatment plan in case there's an outbreak, is that correct?

And, my question is have you contemplated to have a contingency protocol piggybacking for Heaven forbid in case where there is an exposure so it can be a part of the involvement of the product through, that is if (inaudible) by an IRB and FDA, in case there is an outbreak then you could use the agents that's been recommended for treatment?

COLONEL BERTE: The plan is as we move forward and we get to the ability to do a contingency protocol that we would do a contingency protocol and have that on the shelf so that in the event of attack where we didn't have another measure and there's something on the shelf we would have a contingency protocol approved and sitting there that could be put into effect. But that we would concurrently be moving forward towards licensure. So rather than be caught in a situation where we don't

have the protocol on the shelf and now we're running around jumping through hoops trying to do things at the last minute we've got it in place as soon as you need it.

DR. SHANAHAN: I notice in one of your earlier slides that you were showing funding for advance development for '05 it looks like you're getting about a 50% decrease in the amount of funding. Is that a decrease in funding or the fact that you don't have the requirements in advance?

COLONEL BERTE: It's a fluctuation. And, I anticipate it's going to stay up at the higher level, but there was some money that was removed from the palm and that caused some of that dip. But if you look at what the projection is in the out years it comes back up again. So there's not a trend down. If anything again the planning process it looks like we're going to get some kind of a plus up into the program over the palm. Not just for

one year. So I anticipate the curve is probably going to start going up definitely not go down.

COLONEL SHANAHAN: So you don't see that as having any major impact then on the program?

COLONEL BERTE: That dip in '05?

COLONEL SHANAHAN: That dip in '05.

COLONEL BERTE: No.

PRESIDENT OSTROFF: Colonel, when we've been getting these presentations now for a number of years and every year we get those time lines with those little arrows and circles and squares and what we all look for is those little stars at the end when there's actually a product that's a useful product. And, I didn't bring my time lines from previous years to be able to compare what this year's time line looks like compared to the last couple of years. Are we doing better or are we slipping further or what's your impression of where we stand

compared to where we stood a year ago or the year before, because I must confess I keep on looking at these time lines and I don't see a lot of blue stars. And that's what I keep on looking for.

COLONEL BERTE: Well, of course my answer will be completely objective. But I think -- our acquisition strategy has shifted. I mention that, that before we intended to try and get as many things forward as we could, they were ready, let's try and get them out there. Let's try to get multiple capabilities out there. In retrospect I think what that has done it's caused things to slip and I think if we dredged up old briefings and look at schedules we'd see that they were doing just that, slipping along.

We're at a change point here, so I can't predict, but the reason I made the change is I think that it's going to solidify schedules better. Make sure that we do achieve some of

these stars and I hope when you come back next year and you get a briefing that those stars are still in that same column is what I hope this change will do.

You know, can I guarantee that, no. But I'm confident that if we keep focused on our priorities and working in a budget including funding those programs have the highest priorities I think we can stop the slipping.

DR. KILPATRICK: Well, I'll go back and I'll compare the previous presentations. But, you know, I look at these and my eyes glaze over a little bit when I see 2012 and 2014 and 2015 and things like that and you're right when you say by the time we get to 2015 I mean how useful are some of these things going to be and what new things we may have that would relegate them to relative obsolescence, which is really a legitimate question.

So I'm wondering, you know, this

is 2004 and looking at that entire process and seeing, if anything, it's become more arduous and not less arduous. Is this a problem with something on our end or is this a problem on FDA's end or is there a way to theoretically try to truncate some of these activities from your perspective to get something out the other end of the pipe line?

COLONEL BERTE: I think that the challenge is that this is a very challenging process. I don't think that I would point a finger in any one direction and say, "someone's slow rolling the process." The fact is it takes a long time to get these things out. I would argue that the concern with having dated technology is not a great a concern within the vaccine medical products industry as it is within the computer industry.

If you get a product out there that provides protection against a threat agent does it really matter whether it's got old

technology or new technology so long as the capability -- as long as you gain the capability to protect your forces and protect your population that's what's important. How you get there is not as important.

I think that the difficulty is the regulatory process which is in place for good reason and it just takes a certain amount of time to get through that process and I don't think any of us in here, although we would love to see it go more quickly and perhaps there are ways it can be shrunk a little bit, I'm not sure anybody here would want to get up and advocate that we should cut safety or insuring the efficacy of these products.

I'd like to use my kid rule. I put one of my daughters name on it for when I can say would I want my daughter to be using this product if I knew, for example, it was being put out and we had shortcut the safety testing or we had given a false sense of

security because we hadn't done sufficient efficacy testing to make sure that it worked. I think we owe it to our children and we owe it to the nation whether it be DoD or FDA testing or anybody else to put out the best products we can. Unfortunately because we're dealing with biological systems and biological products that's going to take some time.

I know that Congress is frustrated. They proposed legislation, you may be aware of the Rapid Cures Act. Legislation has been proposed that wants to really reduce the process down. It's going to require the DoD and DHS and DHHS to work together to come up with a strategic plan that shortens the time lines dramatically. It's going to tell the FDA to relook its regulatory process. This is graph language. You haven't seen it, you can look at it.

And, so Congress is trying to effect a change to shorten the process, but so I

would say that was a kind of long and soap opera answer, sorry, but I don't see any particular roadblock. It's just a difficult system and we're working through it and we're constantly looking for ways to shorten the process. But there's just so much you can shorten given what we have to do and what we owe to our nation.

PRESIDENT OSTROFF: Other comments? Dr. Patrick.

DR. PATRICK: Along these lines I noted that the radiological item is one that is on the unfunded side and scheduled to be 2010 or '12 or whatever. I'm wondering, the popular media of dirty bombs and availability to these materials, is that interring an attempt to accelerate or raise that the funded line maybe more quickly?

COLONEL BERTE: Yes. It's unfunded because we had no visibility of it the last time we were building a palm (sic) now it's coming down the road and we're putting in a

request, but until that's approved I have to file it under unfunded. But if it's on there, the point is, we recognize that it's coming and we recognize we need to put a marker out there and tell people we need money, because this project's coming down the road and if you want it developed you're going to have to give us some money to do it.

PRESIDENT OSTROFF: Are there other comments or questions? If not, thank you very much and we'll look forward to hearing the presentation next year and I'll bring my time line next year and take a look.

Why don't we go ahead and break.

(Whereupon, off the record)

(Whereupon, break taken)

PRESIDENT OSTROFF: Okay, we're going to reconvene. Let me welcome our distinguished guest Dr. Winkenwerder, anybody who's been watching the news know what a challenging and difficult time this is for the

Department of Defense, and so we're really honored that Dr. Winkenwerder took time out of his very busy schedule to be here. And, it was, I guess, just about a year ago when we received the award from you and it's good to have you here to hear about some of the issues I know the board has been extremely concerned about for quite a while.

Before we turn over the podium, I don't know maybe you want to say...

DR. WINKENWERDER: Once again, thank you for your leadership. I appreciate it. It's been very outstanding leadership and the work of this group continues to be very, very valuable to the Department of Defense, to my office and to me personally. So I wanted to say again at the outset thank you for what you're doing. Thank you for your time, for your service and for your efforts. It's really important.

I came today because I'm

interested particularly to hear about the two topics that I understand are next on the agenda and I'm interested about the presentations, the two issues that's theres a lot of attention, not just in the media, but concern among a lot of people. So we need to hear about that and I look forward to the presentations. Thank you again.

PRESIDENT OSTROFF: Although at times we tend to be a little bit critical I need to say for all of us that we really do appreciate the fine work that's done by Health Affairs and by the services and we congratulate all of you for the things that you do for us.

Let me turn the podium over to Dr. Hoke for those on the board who weren't here at the last meeting you know we had an updated presentation from Dr. Hoke on the status of the adenovirus vaccine reacquisition. And, suffice it to say we left Dr. Hoke a little bit bruised and wounded, but he looks like he's

healed pretty well.

And,, so we're very much looking forward to another presentation. Thank you for coming.

DR. HOKE: Thank you very much. Believe it or not it's a pleasure to be back and I think that we heard really a very good presentation from Colonel Berte in the last hour that was at 50,000 foot level of the chem/bio medical systems and this presentation is going to be very much more down in the weeds for you and in part -- the motive is to address the issue that the devil is in the details, so I wanted to share with you some of the details so that you can see where we are in this project.

The things I'm going to address are going to be your letter first and specific actions that we've taken to address the items mentioned in the letter. The schedule at this time, some of the milestones we've achieved since the February meeting.

I wanted to share with you some details of the critical trial of the old vaccine that was done fairly recently so that you can see what that vaccine looked like in people recently. And, then talk to you about what I see of the acquisition plan risks at this point and then summarize.

In your letter you expressed concerns over the time line, the contact we've had with the FDA, requirements, lack of single and double individuals responsible that DoD could not address the underlying causes of the procurement failure and that the DoD must provide the impetus for adenovirus vaccines.

These were concerns. They didn't require specific action at that time. The things you specifically recommended are here on a high level point of contact with responsibility to the realm of the media to sustain your action with the FDA counterparts so that time frames for vaccine acquisition could

be established. I'm sure that various obstacles can be overcome. And, that this individual will be required to work with whomever necessary at DoD to create a formal requirements document for adenovirus vaccine. And, the board would appreciate an opportunity to review such a document as its next meeting.

With respect to the first recommendation, is going to be deputy for acquisition, but Mr. Howell did the briefing Colonel Rousch in ASD health affairs has been identified to provide oversight and has been in daily contact to check on progress. We have a product manager and deputy -- manager identified in USAMRMC and have formed an integrated product team of our first meeting. We have drafted an ITT charter and this supplements ongoing working integrated product team meetings that were already happening between the contractor and the rare scientists that are working in support.

With respect to the state

interaction with the FDA the contractor had had a meeting with the FDA on the 5th of March, 2003 to discuss plans for the production facility and perhaps I hadn't made that as clear as I should have, but in addition to that the contractor had requested a meeting that took place on the 10th of May, two days ago in which they participated with the FDA to discuss the specifics of the IAV package that was proposed for submission.

My next civil slides summarize the recommendations that the FDA made in that meeting on Monday. And, I should say at the outset, and perhaps you would rather say in conclusion, that this was a little bit of an unusual meeting in that the FDA came to the meeting with 30 or 40 specific recommendations for us all constructive and helpful designed to smooth the road ahead in terms of regulatory bumps.

They wanted an update from epidemiology, very reasonable. In terms of the

general strategy they did appear to accept the notion that the vaccine was a replacement vaccine. They agreed that the 4 & 7 products, which are going to be separate tablets, they agreed that they could be filed under a single I&B and presumably a single licensure application. This is a huge administrative help.

They reminded us that any clinical trial that they might do that we should talk to them first and that will come up later as to why they reminded us of that fact. But that's very good advice.

They were curious as to how the DoD intended to use the vaccine, because the intended use of the vaccine, the indication for it that's in the package insert then becomes the target of the clinical trials and the recommendation for clinical trials and so it's updating -- it would be initial thinking on that usage might fall into the purview of this board

and I'll say more about that later.

They did not feel that as the data had been presented support the argument that neutralizing antibody is a surrogate for protection. In the olden days when the vaccine was developed the tests were not validated as they are today and different tests may have been used and the concept here is if they're going to license the vaccine for protection they're going to ask us to show that it protects.

Now, we're going to specifics of the vaccine those were some comments on general strategy. On the vaccine itself the interest we had in transition for MRC 5 cells later was acceptable, but it would be part of the YND. We can't go back and do this now because too much effort has been invested in the WI38 cells. But we have spoken with Colonel Berte, I guess an e-mail counts as spoken, we have communicated with Colonel Berte on taking advantage of some MRC 5 cell experience that CDMS has and we might

get some acceleration there, but that's a downstream issue. The request is specific tests on the WI38 cells to demonstrate -- nature. They suggested a specific TCR test to be sure that there's no cross contaminations in the vaccines and they advised some tracking pedigree of cells to be sure that there was no possibility of exposure to BSE.

On safety data they wanted us to bring together any old safety data that might exist from DoD experience. We're really at this point not entirely sure if we used the vaccine in women, although there is one report that suggests that it may have been given to some recruits; some trainees, and because of the way the immunization records were kept at the time and particularly the way adverse events may have been reported the information is very diffuse. It may only be in people's shot records, for example.

So this will take some doing and

they will certainly want post-marketing surveillance data on females once the vaccine is licensed. This comment on safety, I said current, but I really meant they will want safety data on at least fifteen hundred recipients of the vaccine during clinical trials and they want to know how the vaccine will be used with respect to the young women trainees later. Those are all safety issues.

They made a number of comments regarding the clinical development plan. The statistical basis for the initial trial. They commented that we said the trial would show safety, but then there wasn't any discussion of the study size based on an analysis of what safety we wanted to show. It sounds like a picky point, but what they're saying is, "why don't you do this, so that when we're reviewing the results we won't have a question. We want it taken care of now."

Issues about -- some issues that

we may take exception to assuring that spouses of basic trainees are not pregnant is a very, very difficult and not practical thing to do at all. We may have to have further discussion with them about that. Concern over pregnancy issue again and how will we take care of that. That's subjects of the history of GI surgery be excluded. That's a helpful suggestion so that we don't have complications that arise that might be attributable to the vaccine that's orally administered. And, a number of other issues, stopping (inaudible) of the study. A number of other technical issues.

The most important one is that they did request a study that demonstrated efficacy and suggested that this didn't have to be a massive study, a figure of maybe three hundred per arm was mentioned with a relatively easily identified case definition, hospitalizations due to adenovirus infection and upper respiratory symptoms or something like

that in a procedural controlled trial is what they were looking for.

They were trying to tell us they wanted it, but it wasn't going to be too bad. The inpoint assays they suggested that we use a PRNT50 instead of the TCID 50 assay for antibody testing. This seems like an incredibly -- virological point. But the idea is that in a virologic assay a fact reduction -- in a fact reduction assay you're actually showing inhibition of viral replication and viral particles. In a TCID assay you're showing that no single virus particle remain uninhibited and so by nature the PRNT 50 assay is more sensitive to antibody.

Again this is a hint, hint, they're saying use this kind of assay instead of that kind and they of course wanted permission about the assays I mentioned by this case definition.

So just to pause for a second and

say then in response or in association with your recommendations that we have these discussions with the FDA, that meeting has taken place and as you can see it was filled with recommendations, all of which will be very helpful in smoothing the way forward, which I think was the intent of the recommendation.

Now, the board recommended that the individual be empowered to work with people within the DoD to create a formal requirements document for adenovirus vaccine. And, would appreciate the opportunity to review such a document.

Immediately following the last meeting the Deputy Director Physician Mr. Howell did request requirements documents from the (inaudible). Our liaison down there, the MRC... liaison Dr. Nelson is working with them. And, the priority to the moment has been to generate a place called an initial capabilities document. This is for all infectious disease products and

the specific capability production document for the adenovirus vaccine will be done after that, so I don't have that to show to you. I guess it would be made an open issue.

MEMBER: They acknowledged that they were doing it. It's not a case that we have to convince them any more, they're convinced.

MR. HOKE: Right. Now, there was another recommendation that he made on the diagnostic testing and approved antiviral treatments, and I must say I confess that this is to be dealt with not as great detail as our concentration on the vaccine. We've looked on the FDA website and found that there are a number of assays for adenovirus infection that might be useful. In addition the folks at WRAIR have been developing assays that will be intended for the clinical trials of the vaccine. These might be useful.

The drug picture is considerably

more murky. There is one drug, Cidofovir that Dr. Huggins here at USAMRIID mentioned to me and I found one paper and I'm sure there are others where it was promising a (inaudible) model, but this is obviously a long way from use and approved for our trainees.

So we really don't have a strategy for implementation for this recommendation yet. We really don't have any wherewithal to do anything, but I think we really -- I know we certainly owe you a plan for how we would approach this recommendation in the future.

Now, the last time it was the schedule that really attracted attention and so unlike Colonel Berte, I'm showing you the schedule that I showed you before.

So here's the one -- of course it was the 2009 issue down here and we went back and looked at this very hard and we tried to identify areas that we could squeeze it, better more manage the time more tightly and we -- this

is now our working chart and it calls for licensure in 2007, which is what you have been told in the previous briefing and I think we can do that. We can do that if things work out and it's likely to be complicated, but we took out some intermediate trials I think if you really went back and compared -- so we're really going to be planning two sets of trials, an initial trial and a very much larger trial, but still honestly hasn't been designed, because we just got our guidance from the FDA on Monday.

By a trial that will look at efficacy inner basic training folks and then also the 1500 safety data will probably come from that environment as well.

Now, the next several slides I have are really just our -- just to show a little more detail for each of the major areas that are in that first gant chart. It's probably just to remind you that actually we have done an awful lot at the time of the last

presentation. And, honestly I dare say more than we've ever done on anything before. You know, you actually have, through the contractor have built a production facility for the (inaudible) part and, you know, that was all planned here and the equipment's been installed and validated and so that's, you know, we had to have a facility, so that was good news.

To work on hylic and GNP (sic) tablet production is all planned and those steps are taking place now. The regulatory issues, all the steps in terms of draft IND has been written. The company is planning to file the IND on the 1st of June. That's just a few days away and they are having to adjust that filing based on what was told to us in the pre IND meeting here on May 10th, day before yesterday. So you know all these things we're trying to work them all together.

The clinical trial work in Phase 1. The clinical trial with all this information

shows the preparation of the protocol. The protocol was approved by the HSR (inaudible) implementation in March. There's going to have to be some changes to it now based on what the FDA told us. And, that may take -- that'll take some time to make the changes and then they'll have to do whatever needs to be done with that. But the team has already gone down to Ft. Sam to meet with the commander down there and begin I think to identify the population for that study which will be the 91 Whiskey group of soldiers. And, they're down there today, in fact, collecting blood from cohorts to learn about the prevalence of antibody adenovirus in that group as the trial goes forward.

Then the planning all the way through the final study report that's shown here, these are the details. The tablet in production then becomes the next big issue for the Phase 2 pre-clinical trial and that is outlined here along with the planning for the

Phase 3 pre-clinical trial, which I said earlier hasn't actually been done yet. But it's part of the process.

Then finally the regulatory affairs package and submission for the license agreement out here in Post 7. That plan has already been done.

So that's the overall plan again, this is the same slide as you saw before and we think that we're reasonably confident that this has been planned in a level of detail that will allow us to actually do this by 2007.

Now, I just wanted to mention a few milestones that I've actually already mentioned about them except to tell you that we did get a quarterly report from the contractor and I'm going to go over that with you in a minute.

I've been meaning to tell you about the Phase 1 and 2 clinical trial. And, the contracting issues are important and because

we worked through USAMRA, the U.S. Army Medical Research Acquisition Activity, and they are included in our integrated product team so that we can make sure the contracting issues are smoothed out to the extent possible.

Of course, the government has its rules and regulations and has to follow the law. And, the company has its perspective on things and we don't always agree, but we can try to work them out through our contracting officers.

Now, the contractor's quarterly report is where we find out just what progress is being made. These are the issues that are dealt with and these are the same issues that I presented to you before, but this quarterly report, the bulk virus production, the formulation and -- assay development tablets, trials, DoD issues from the company's point of view and financial issues.

Now, the both virus production issues which the (inaudible) virus were tested

and passed all of these tests. You know, the passing of the test means the substance wasn't there. Or that the materials were identified correctly, so that's good news and good progress. The ADV-7 GMP lots for vaccine production have been done and have been saved. The type of lot that was made in October was titer and the titer was sufficient metal for vaccine production and the infiltration step you often lose a lot of virus when you filter it. Very little was lost at this time.

And, that has been sent for storage for later transferring to the facility down in Virginia. A whole bunch of tests were done on the adenovirus and the results were satisfactory. For the ADV-7 similar work was done, although in this case they needed to make a replacement batch which was done and shipped to WRAIR in January with titer for ...zation, and it passed all its tests as well. So that's GMPADV- 4 and 7. The next step is the

formulation and authorization and for the ADV-4, the run was done in 8000 doses which was (inaudible) produced and stored at WRAIR and that will be shipped to the Virginia facility, and similarly in February (audience noise).

Assay development is being done largely at WRAIR. ECR tests where the validation is ongoing. They tested a number of specimens from the facility and it indicates that the screening program is adequate to proceed. Assays for clinical trials are under development at WRAIR as well.

The technical things like an antiserum you need to show you got the virus you think you've got and not other things. It requires that the company use the old serum from (inaudible), but that new serum be developed as well. That's being done and the methods for inactivation for virus in the production area are being evaluated.

The tablet production facility

further downstream has made progress. The pilot batch of tablets has been produced. No loss in titer and the (inaudible) contents were above expected values. The tablets failed the disintegration test. These kinds of things happen. They're part of the development process. They need to be dealt with and those issues are being dealt with.

There was a small problem in the tablet equipment that has been corrected in two pilot batches or have been made and are being evaluated. (audience noise) has had a problem with the solvent content that was too high and too rapid disintegration of tablets so that protocol is being modified and the FDA performed a GMP inspection of the facility in April for other products, but their quality systems were included in the inspection and they passed.

On the clinical trials I told you about the CID meeting and the two trials that are proposed, one trial will be done at Fort

Leonard Wood and an additional thing I might mention that at Fort Sam and the larger study, the MES... Study will be done at Fort Leonard Wood though we may seek other sites for that.

It's not entirely clear or we haven't decided or the company hasn't decided who exactly will do these trials, but that will happen soon.

Now, the company, and this is a report to us again as noted, and the AFEB and ASD (inaudible) interest. There was a scope change that they proposed based on additional items and that has taken some time, but I think that has moved along well now.

The contract had an option in it for the Phase 2 and 3 trials that was going to be several years from now, but that option was exercised in order to reduce the amount of time that the company would have to spend getting those things done. We've had an issue related to billing procedures that is currently being

resolved through negotiations.

So the point of the last ten minutes is that the company, the contract company that is working on this vaccine has filed a report and for the last quarter and that the details, I warned you this was going to be down in the leafs, this is down in the leafs of the vaccine development and effort are proceeding and proceeding fairably. There are bumps in the road, but when you get down to the real world those kinds of things always happen.

So I want to spend just a little bit of time to tell you about a clinical trial that was done on the old vaccine in 1997. This was done at WRAIR when it was realized that the vaccine was not being manufactured any more and the folks down there had the view that well it might be useful to do one last clinical observation with this vaccine. The hope being that it would serve as kind of a bridging study on to the new vaccine. Even though those

tablets were expiring there wasn't going to be an opportunity to do a contemporaneous comparison.

So this trial was done and called the characterization of the serologic and biologic responses of healthy adult volunteers and it was done by Colonel Kuschner and Colonel Sonn (sic) provided these data. The vaccines were the approved 4 and 7 vaccines and the purpose was to provide a bench mark for comparison of a replacement vaccine. It was done at WRAIR with healthy adults and neutralize the antibody was evaluated along with symptoms.

40 people enrolled, 5 were excluded in the enrolling period due to the development of antibody and 1 lost at follow-up, so 35 were actually analyzed and they broke down like this. None of them had antibody in both 4 and 7, 8 had antibodies to neither; 5 had 4 only and 22 had 7 only so there was kind of a mixture

of past experiences.

The seroconversions which is defined as going from a a sero neutralization titer of less than 2 to more than 2 was 90% and for the adeno 4 and for the adeno 7 it was 100% according to these definitions.

And, this was the distribution of titers of the ratio of titer. Well, since this was the seronegatives to start with they were essentially all divided by 2, that's why there's less than, the sign is here. But there were relatively low titer range actually in this trial.

And, they looked at shedding and feces and adeno 4 and adeno 7 were shed by all of the recipients of the vaccine, though none had that virus in the throat cultures. And, this was for a fairly long period of time and in some cases the shedding hadn't stopped by May 28th. So that is an issue.

The symptoms that were reported,

and this is an uncontrolled study, were a distribution of things but there were a few upper respiratory symptoms in 12 of the 35 recipients.

So now remember at the beginning I told you that the FDA made a comment that they wanted to know about things ahead of time. I told you that later I'd explain why they said that. Well, what they said was right out off the bat in the beginning of our discussion they said, "well, did you talk to us about that study?" And, there was an admission that they had not been talked to. And, they said, "well, you know, we think that the study is probably too small to really anchor your program and in the future you should talk to us in advance."

So it was -- this was done several years ago and, you know, it was a licensed product and at the time I would have to say that this what seems obvious in retrospect issue wasn't so obvious. It was not obvious at the

time and it's a lesson for the future.

But it partly led to the wish by the FDA that instead of using this as a comparison with which to license the vaccine met actual clinical trials demonstrating efficacy with the titer.

So I wanted to switch then from that set of slides and also talk to you a little bit about what I see as risks in this program. The main factor is I think is pretty far down the road, the contractor, in identifying a production facility for the virus material. Remember the facility in Virginia is for tableting.

My opinion this is not a perfect arrangement yet. Optimally there would have been a building right next to the tableting facility. That is not the plan. And, it turns out it's fairly difficult to find companies willing to make infectious material in small amounts for you as this company, as a company

would have to do as a subcontractor.

The contractor believes that this problem will be solved, but I would say until it is solved it's still an open issue.

The clinical trial program, the addition of the efficacy study may increase time line and costs, but I'm hot a hundred percent sure of the time line. The costs -- the technical issue here is that the contract with the company calls for safety in immunogenesity studies, not efficacy studies. So there's a fine point there that will need to be negotiated and there may be additional costs in the study for that in the development program.

We have a time crunch to get the changes made to the protocol. The protocol is now scheduled for implementation in September. If we miss that September window, because of the winter holidays we'll be pushed until after December for starting that trial. And, so there's a large incentive to get everything done

by September, but there's also the regulatory review of the changes that have to be done, so it's going to be tough. So that's an issue that may cost us a few months.

We then identified the clinical teams for the later study, so that's an open issue. The serological testing, validation of the test has not been completed yet and so again that's an issue that we have not resolved. The site for testing a large number of testings needs to be identified as well.

And, also I didn't talk too much about this, although I alluded to it, the issue of female trainees. The issue of reproductive toxicity studies has really not been resolved. The FDA is looking for our thoughts, I think it's as much theirs as to how we can address this issue in a responsible way.

So those are risks that are open issues in the trial and development process, but I felt that I needed to share with you. We have

additional acquisition steps that we want to do to tighten this program up. I think what Dr. Berte showed you was a pretty tight idea of how vaccine acquisition should be run and I think we're doing a good job. We talked about the capability production document, the charter for the product manager is in the works. We've done the integrated product team in meetings and the charter is in the works for that. We need to -- now that we've got FDA guidance to complete the test plan. We have never dealt with milestone review on this product; partly because it's being funded by a different way than many other products. But this is something that we need to do so that the milestone decision authority, who would be the commander of MRNC, you know, would have the formality of this briefing done, not that the briefing itself is just proforma so that we've looked at all the issues and assure him that -- or inform him of what the issues are. That's an important

acquisition step. And, we need to look into the future on budget authority.

So I know you're all wondering what you might do to help and I'm sure you have ideas completely beyond what I can think of, but I thought of some of these.

Since you all are functioning as kind of an over arching IPT, innovative product team. You're also kind of senior advisors to the DoD, but you know by asking me to come here, you know, sort of checking on the process and I think that's valuable for you to do that. For one thing, you know, it gives me a hammer, if you will, to go back and say, "no, we absolutely need that quarterly report. We absolutely need this information because the IPT has asked for it," or asked for an update. So that is useful.

The use of the vaccine, remember I alluded to this, the FDA asked us about that and, you know, we have a notion, the company has a notion, and there were policies before, but

the board may wish at some time as licensure approaches to give some thought to what the policy would be so that to make sure that we have a vaccine that will do that when we finally get there.

And, also this issue came up and I first was very nervous about it, but I felt kind of duty bound to bring the idea up and I'm glad I felt that, because someone asked a question very similar to this before. You know, would anybody recommend that we should have a treatment IMV at some later time. Once, you know, the studies have been completed and relating licensure, something like that, I would say it certainly should follow a time where convincing evidence of safety and immunogenicity and probably efficacy have been produced. We don't want to rush into something when we haven't got it yet. But that's an item that may be discussed in the future.

I mention this 21CFR B12 because

that kind of talks about the specifics of the ...IND. I'm not suggesting that we should, but I'm just saying that somebody might think of that.

So, the effort is advancing towards its goal. We're working to kind of mold this into the DoD and Army acquisition model. The contractor is making progress. The FDA has provided detail guidance. Many problems remain to be solved, but we don't see any unsurmountable obstacles. We do have a company person here also to show this...

So, now this is the vision. I'd have to say that I've been involved in a lot of product development efforts in the last twenty-five years and this really isn't (inaudible) this is a lot better than most of the things that we're doing. I'm not sure that it's betterness is what was being referred to, but we are taking this seriously and we are moving ahead. We've never actually built a facility

before. So this is way out -- we've never actually been involved with a product where the DoD has really and truly taken full responsibility for. So it's not -- it's business that's actually in many respects better than usual. And so that's all I have to say.

There's some ambiguities in this last slide, but I think I'll just... maybe it's telling you that I think we're on target or that I am the target. But I'll be happy to address any questions that you might have at this time.

PRESIDENT OSTROFF: Dr. Hoke, thanks for a very comprehensive presentation. I'm sure all of us around the table appreciate the complexities of this process and what you're undertaking. Before I open it up to the board for questions, because I know that there are a number of individuals around the table who have expertise in some of the trial designs and some of the issues that have been raised and I know that there are representatives here from the

company and we very much appreciate them being here for this meeting and I was just wondering if any of the company representatives would like to pose any comments. Dr. Tollis is here. I'll introduce Dr. Tollis. He is one of the principals of the company called Maccgen that is a subcontractor for this project.

DR. TOLLIS: Thank you very much for the opportunity to have Charlie present our slides. I think that it's been an interesting development program for many different perspectives. I think the one thing I'd just like to point out is that it was the original vision as a tech transfer project and that is really quite an underestimate of the amount of work that we've done over the past few years and ultimately I think making good progress as has been outlined and as Charlie mentioned we had a very good meeting with the FDA and they seemed to be working with us. And, I'll be happy to answer any of the technical questions about the

vaccine.

In recruit settings and it strikes me as being inconceivable that no one would have data about its use in female recruits. And, I'm really quite amazed that that has arisen as an issue and I'm just wondering if anybody in the front might want to comment based on their prior experiences, because I know a lot of you have been in the service as preventive medical personnel for a lot of years.

DR. TOLLIS: While you're thinking I'll just say that the concern is that we diligently and documentatively have looked for such information.

DR. KILPATRICK: Have you got any comment? You've had more experience than any of us probably.

CT. RYAN: Well, it's surprising how little data we have on female recruits because in the earliest years of vaccine use women recruits weren't vaccinated in all the

services. Navy didn't begin getting vaccinated until '94, so we went from '94 to '98 or so when the vaccine ran out that female recruits were vaccinated. The number who were pregnant is very, very small because all pregnancy tests were done before vaccines are given. The number, I estimated it as something like 40, at the most, all services wide per year between those few short years. And, all of those women became civilians very quickly. They're not followed in military corps what happens. They're all counciled about the fact that they received some vaccines while people didn't know they were pregnant and they're quickly separated so we have surprisingly little amount of data.

COLONEL GIBSON: This is Colonel Gibson. Back in '85 - '86 - '87 at Lackland Air Force Base working as (inaudible) in basic military training. And, anecdotally I can tell you that I watched females come through the immunization processing system my flight right

after they mixed in with the males. And, at that time they all took their pills, went out to a water trough outside, got to drink some water and moved on. And, I saw them go through that exact same process that the males did at that time.

As far as documentation I have no clue at that time the documentation of vaccines were going strictly into the shot record. They probably have log books that show what flights were processed on what day, but as far as having whether the females received that adenovirus document is problematic.

Our process within the Air Force is exactly the same and -- talked about females were tested. As soon as they got there on Day Zero those that were ACD positive were separated. We tried to do it in such a way that they did not receive any live virus vaccines. But they left the service immediately.

PRESIDENT OSTROFF: Let me open it

up to comments and questions and in particular I know Dr. Gray probably has some thoughts as far as the recommendation about assays and the things -- the vaccine is available. I know this was particularly an issue that he wanted to insert a recommendation.

DR. GRAY: Wonderful summary, Charlie, thanks so much. I guess my concern is, is we're looking at tremendous morbidity numbers by the Naval Health Research Centers data, 1400 and some odds unnecessary medical encounters which translates to a significant proportion of hospitalizations and an importance portion of intensive care units and likely 2 deaths per year. So if we take that out to 2007 that's a whole bunch of variable morbidities that we need to think about. I'm thinking with respect to the treatment question, certainly that's probably not appropriate for the product management team, but our thinking was that we engaged some of the clearest thinkers in

infectious disease and the DoD internal medicine to review the bone marrow transplant literature, which does have a number of publications evaluating treatment and compromise patients come up with a rapid diagnostic strategy and a treatment perhaps under IND at these facilities such that you would have a chance at saving some of these lives and severe illnesses.

It seems like a logical thing to do with this projected time line and I would encourage you to engage, especially advisors in reviewing that literature.

There certainly are some wonderful very easy to use point of care rapid diagnostics that even in our not really complex training centers we could easily use those and say yeah, it's an aveno, he or she is in an intensive care unit. Let's engage the algorithm and offer whatever treatment we can besides that which is simply supportive.

DR. HOKE: Your point is well-

taken and we can do more in this area and we will do more.

MR. KILPATRICK: Charlie, can I just say what prevents us from bringing a team together and being able to look at that and ask Dr. Gray to be a part of it?

DR. HOKE: What prevents us?

MR. KILPATRICK: Yeah, I just don't see at this point why there's no reason why we can't put out from (inaudible) put together a one to two day sort of group that looks specifically at that and Dr. Gray would be a part of it and let the group then come up with what they think the treatment routine or algorithm or what those are.

For us to go back and do development and stuff it's probably not going to mean we're timely or anything else, but if we're looking at something that is there, that we're looking at other indications or at least some knowledge base that we can go directly into an

IND then it would be...

CAPT. RYAN: Actually I have one comment going back to the toxicity, I guess a couple comments on the slides were that this (inaudible) I think that may be an underestimation I think there are going to be required and I think probably looking ahead right now to clean up the strategy of how that is going to be looked at, whether or not it's done at this point in time or a year from now or the next year I think we should have some kind of a time line for things to take place. I think we need to come up with a plan as to how that is going take place...(audience noise)

PRESIDENT OSTROFF: I think that's an excellent point. This is a different era than the last time that this product was licensed. So I think it's probably correct to say that we're going to presume that that will be required.

The other issue of the serigence

of, you know, the VEE (inaudible) antibodies... the BW vaccine this is a situation where this illness is basically causing an epidemic in virtually all of the recruit settings and, you know, the importance of having solid epidemiology data, I mean the bottom line is whether or not the product is actually working. Is the audiency respiratory rates of respiratory infection rates dropped like a rock. And, that certainly was the case when the vaccine was being used and when it was not being used they went up like a rocket and so, yes, it's nice to see all those other markers, you know, showing antibody responses and I know the FDA likes to see all that, but the bottom line is this is pretty easy to tell whether or not the vaccine is doing the things it ought to be doing. I don't know if anybody else has any thoughts about that.

MR. MALONE: Joe Malone, DoD GEIS. I have a comment and recommendation. With

regard to that 1997 study I'd like to say that I compliment people who did that, who had the foresight to do it. There weren't a lot of resources available at that time and I think they did the very best that they could with what they had available.

With regard to the future I think there are several things that we need to consider in addition to possible antiviral in the female reproductive studies that could cause us problems.

With regard to the immunogenicity studies, Charlie, if we find ourselves losing time on that and getting into winter respiratory disease season we may have a lot of trouble finding an installation where we're going to be able to -- measuring because of circulation virus.

That's a study that I think would have greater chance of succeeding if it was done some time in the summer or outside of the

respiratory disease season.

With regard to the efficacy that also concerns me that the FDA is now talking about efficacy, because the issue that we have been concerned about is that prior to the vaccines, prior to 1970's antivirus type was predominant in adenovirus 7 emerged when 4 was suppressed with vaccine. And, one of the questions that we have entertained is how would we approach an efficacy study for Type 4 and Type 7 vaccines when we aren't seeing Type 7, but we would expect to see Type 7 when we suppress Type 4. If we had to go into something like a two step efficacy trial that would be a lot of time on your time chart.

With regard to the reproductive studies, the productive antibody levels I think Dr. Ostroff relate to the comparability issue and if we're going to have to deal with that, then there may be a way that we could use banked sera somewhere and look who developed disease

and who didn't and then also with regard to the BNL issue I think we need to consider whether or not we will have to attempt some sort of a look back on that and get documentation and try to identify exactly what happened. All of these are important at this point in time, because of the amount of time that they would require in the future and the impact that would take on the time line.

So I would suggest that in addition to looking at the antiviral question, that we address all of these perhaps in different groups, or maybe in the same group, and look at whether or not something should be done immediately to move ahead on these and also to look at what would be involved if we later down the line what impact these studies would have under time lines.

DR. HOKE: The FDA was aware of the issue related to the adeno 4 being the principal virus now and that adeno 7 would come

after we used the adeno 4 vaccine which was the observation before and the complication that provides in designing comprehensive clinical trial.

They seemed to say though that we really needed to -- we needed to go and do it and see what we found and that if we could show that the adeno 4 vaccine was protective and establish at the same time sort of the immunological correlates, you know, just exactly with today's tests what level of neutralizing antibody was associated with, you know, a zero attack rate, for example. That that argument might be advanced to the adeno 7. In other words, there would be much more substantial data at that time that we knew what level of antibody was protected.

It was a little bit, it was left a little bit vague. Dr. (inaudible) did you hear that any differently?

DR. : That's quite correct.

DR. HOKE: So I had the distinct impression that they weren't going to be asking us to do something that was, you know, practically impossible in a reasonable time frame. That is you wait until adeno 7 emerged and then show that we had efficacy against adeno 7.

PRESIDENT OSTROFF: One more quick question from Dr. LeMasters and then we're going to have to move on to our other issues.

DR. LEMASTERS: This question that I have no idea about, but when we talked about female reproduction I also know that the -- involving male reproduction and we know about shedding the secal culture, how about semen culture, is there any information out if the virus would be shedding in semen and if so what about the exposures to women, their spouses, etc., and is there a concern about, I don't know what the concern was about the pregnancy, if the spouse was pregnant and they were concerned

about exposure was that because of possible shedding in semen or oral or something else, whatever it is, I think we need to at least know why there is a concern and how we can educate and caution our recruits in possibly exposing others. You have to think about human sexuality in its entirety.

DR. HOKE: I think that the points are excellent. We have a complicated situation where our intent is to use this in recruits, where I'm under the impression that the policy is there's no sexual activity allowed. And, that seems -- I have never myself been a basic trainee myself and I do think that the trainees are released at some point, they're not incarcerated, so we're going to have to look at exactly how the vaccine would be used and address those issues in terms of what risks one might imagine.

PRESIDENT OSTROFF: Thanks very much. What I'd like to say is we really do

appreciate your work and hopefully in the not to distant future the recruits will thank you and their families will thank you.

Let me turn it over to Dr. Winkenwerder before we move on to the other issues.

DR. WINKENWERDER: Thanks, Steve. I appreciate the presentation we just heard. I also appreciate the AFED's concern about the adenovirus vaccine program. From my vantage point your involvement and your concern is helpful. It's very helpful. The schedule and timing that was laid out in the past you had, as members of the board, the same reaction I did and in that that that was not acceptable. And, in a meeting a couple of months ago we had in my office I made that clear to General Martinis and Dr. Hoke and others.

It appears we've made some progress, some real progress, most particularly in the last two or three months. I know there's

been work that's been going on but we seem to have more of a clear game plan now.

I did have a couple of questions just before I leave I want to make sure I understand. The leadership is clear within MRNC in terms to product manager. I didn't hear you identify who that person is.

DR. HOKE: Yes, sir, it is clear that Mr. Howell is the focal point and Dr. Lightner works for Camden, any ambiguity that there is directly been due to the ambiguity of my employment status as contractor versus...

MR. : We're in the process of making contractors government employees so that is controversial, but there is clear accountability there.

DR. WINKENWERDER: Okay. And, also are we clear about who has accountability for your ICD and CPD documents.

DR. HOKE: Yes, they have been requested from individuals by name.

DR. WINKENWERDER: Okay. And then, let me finally add my voice to I think what I've heard in terms of prudence of rapidly pulling together eighteen people to look at the matter of rapid diagnostics and rapid diagnostic and treatment algorithm as something that's in here a measure that we ought to do. I will be glad to ask one of my staff to task this issue to be sure that it's clear it needs to be done to General (inaudible) and General Martinez, and others, but I think we're in agreement that that needs to be done and quickly.

I also would agree that getting pregnancy toxicity studies done or a plan for that seems to make a lot of sense.

The last couple of issues I'd just say is being able to use this potentially as an INB product I would ask AFVP to think about that and give us some thought and recommendation about that as well as the other questions that were teed up for you. Go ahead from my vantage

point and do those, address those questions that you've been asked to address.

And, then finally for you and Mr. Howell I would ask you to identify now any -- even if it definitely don't come to pass, funding issues or shortfalls or gaps or whatever. Because our budget process is a long drawn out kind of thing and we need to identify those issues now and not have to deal with them in a short crunch time when it becomes harder to move the money.

So with that I'm going to say that I'd like to see that we make every effort to meet this schedule or beat it and frankly get something available sooner in terms of approach as it relates to diagnostic and antiviral treatment regiment. Because I've had concerns about the morbidity and mortality associated with the adenovirus.

If there's ever any (inaudible) on this, if people look back on it they're going to

have to ask why did all of this happen and we only can look at ourselves. We are collectively responsible, so let's keep it moving, let's get the job done. Thank you.

PRESIDENT OSTROFF: Thank you, Dr. Winkenwerder, for those comments and for your leadership on this issue. I know that you were also very interested in the other topic. This presentation will not be quite as long. I will say that we've had some fairly extensive discussions about these recommendations yesterday in the afternoon and there were some modifications made, so I'll turn it over to Colonel Phillips.

COLONEL PHILLIPS: In response to growing concerns about the safety of use of mefloquine from the media and congress and service members Dr. Winkenwerder asked that an AFEB commission, a sub-panel to look at developing study formats for looking at adverse effects of Mefloquine and that subcommittee met

one month ago today on the 12th of April. It consisted of AFEB members, DoD and non-DoD experts on malaria, epidemiology, neuropsychiatric disorders and pharmacology.

The questions that Dr. Winkenwerder specifically wanted addressed are on the screen now. The medical literature describes well adverse effects that are related to Mefloquine use including rare serious adverse effects such as psychosis and seizure, but the literature does not describe the military cohort, particularly a military cohort that's deployed in an operational setting at which point some of the normal reactions to a combat setting such as stress, anxiety, depression, many confused with side effects of the medication. So it was important to look at compare to breaks of adverse events, including neuropsychiatric events in the operational setting and the question before the board was, what's the best study -- protocol study design

to be able to answer these questions adequately.

When the board met they were presented with information on the historical experiences of the military with malaria and malaria prophylactic medicines. They were presented with pertinent data sources that are available to us in the military, including personnel registers, help encounter forms, how help encounter forms are recorded in operational settings. Post-deployment health assessments, how those are recorded and tracked through our surveillance mechanisms. And, the DoD serum repository as a source of data and information.

Additionally they received briefings on our pharmacy data sources. The board was particularly impressed with the electronic and data sources that are available appearing in the COMS and the MTS pharmacy data transaction systems and CHDS. They did note challenges that DoD faces in accurately documenting prescription medications in

operational settings in the combat areas.

The board also received briefings on DoD mortality surveillance projects and suicide surveillance activities as well as a brief on millennium cohort study with suggestions of how that data source may be available to assist in developing a study looking at adverse events from Mefloquine.

Finally the board reviewed rather extensively the medical literature that's available currently on Mefloquine on adverse events related to Mefloquine and other anti-malarial in coming up with their recommendations.

To get right to the heart of the matter the board recommends that before we specifically address the two questions a careful and well-designed descriptive setting of the health outcome potentially related to Mefloquine begun as a prerequisite subsequent analytical studies. Do this first is the message that the

board sends.

The focus will be on documenting specific measurable outcomes. The board noted that adverse events such as side effects, headaches, dizziness, vivid dreams, nightmares, are of interest.

They are suggestive in nature and they relate -- their relative importance in an operational environment is hard to determine. Rather what the board recommends for this study that the outcomes that are looked at be hard, measurable outcomes in addition to the traditional outcomes that are measured in a study such as this in death and hospitalizations that the study also looked at deployment-related outcomes such as evacuation from -- and loss of duty time, as well as other sources of data on outcome such as criminal violence, attempted suicides as well as completed suicides and other medical problems such as retinal damage or odor toxicity which can be documented.

Finally the board did make a point that an adverse outcome associated with mefloquine use is also malaria, because if a service member is not using the medication because of concerns about the medication and develops malaria, then that would be an adverse outcome that's of interest to us.

The board emphasizes that the underlying issue for all of this work is malaria and in the prevention of a very serious illness amongst our service members.

To address the first question that Dr. Winkenwerder asks regarding adverse events the board recommends either a retrospective cross-sectional or a prospective cohort study approach. The advantages of a cohort study approach are that a cohort study designed to assess multiple outcomes to one or more exposures.

Given the number of personnel who have taken mefloquine and OIF and OEF the most

feasible of these options would be a retrospective cohort. A prospective cohort would have problems in that the measurable adverse outcomes which we're interested in are relatively rare and also considering that -- OIF2 mefloquine is essentially not being used in Iraq anymore based on entomological and epidemiologic surveillance. A prospective cohort could take several years to acquire enough data to come up with measures.

So the board recommends the most feasible option is a retrospective cohort study approach. The key in this study will be identifying a measure of exposure to mefloquine and the board recommends that an index of anti-malaria -- mefloquine and other anti-malarias that an index be developed that uses multiple data sources including paper medical records, log books from battalion aid stations, the electronic data records that we have, health assessments, and even a serum markers using the

DoD serum repository.

The hazard that is inherent in this approach that needs to be watched for is the potential for a misclassification bias, exposure due to compliance-related issues that are uncertain at this time.

To answer Dr. Winkenwerder's second question regarding suicide. The board notes that because of the rare nature of suicide and the large number of variables that are associated with suicide, the complexity of studying suicide, that the best approach to looking at this would be a case control study design. Case control study design allows you to assess multiple factors that may be associated with a relatively rare outcome.

The important points that the board emphasizes with this approach are that a carefully constructed case definition is critical. The board noted during the presentations on DoD suicide surveillance that

it's often -- you're talking gray areas and fussy areas in determining if something is actually a suicide or not. So that's an issue that needs to be carefully crafted in such a study.

The board also recommends, because of the relatively rare occurrence of suicide, that this study -- that those who undertake this study would look beyond just OIF and OEF and may be looking at previous deployment experiences and search for data there as well.

The board recommends that in this case control study that multiple control groups be used, including for your control groups deployed personnel who have returned home safely and deployed personnel who died from other than suicide as a cause; whether it's combat-related or medically-related.

In order for this study to be valid it's critical that the control groups be assessed as rigorously for factors potentially

relating to suicide as to an equal degree as the cases are studied.

Other miscellaneous recommendations from the board that are detailed in the draft recommendations. The board recommends, using as a data sources or exploring more fully the use of the millennium cohort study, as I mentioned before, that's because the millennium cohort study may use a baseline mental health and psychological factors which are already measured or being measured in the population.

The board also felt that there would be some significant advantage to developing a methodology that they would be able to use the serum repository for objective markers and objective proof of mefloquine exposure.

The board also recommended and noted a member of the AFEB who serves at the VA was present at the subcommittee meeting and

noted that the VA is also looking at mefloquine because of their patient population and is looking at doing long-term settings on potential outcomes associated with mefloquine use. It would be important for DoD in funding this study to make sure that we're coordinating our efforts with the VA with the potential for even having a cohort with data that we could hand off to the VA for their use and long-term and ongoing studies.

The board finally recommended that the study be transparent. That it be overseen by a non-DoD oversight board. That non-DoD collaborators work with DoD investigators on this study in order to insure that the results of any study has credibility amongst those members of our service members, of Congress and of the media who had questions about DoD's responses to our issues with mefloquine.

And, finally, the initial study that's recommended looks at potential

associations with mefloquine use. The two studies that were recommended, to answer your questions, look at assessing causality or a potential of causality with mefloquine use.

The board also recommends that we take that to a third step and not just assess the association of causality, but look at ways we can study that may be helpful in terms of intervention to improve our health outcomes; whether it's in preventing malaria or reducing side effects. And, in particular, the board acknowledges and encourses DoD to pursue the knowledge, attitude and beliefs in compliance types of studies that we've discussed at various points in time as well.

PRESIDENT OSTROFF: Thanks very much. That was a very nice overview of the discussions.

Let me open it up to the board members, because I know that there was a fair amount of discussion of this yesterday and

particularly those members that participated in the review last month. Dr. Herbold.

DR. HERBOLD: Steve, congratulations on a wonderful presentation on highlighting the systematic approach that the board thought was necessary.

I just want to emphasize again that I believe there are probably other data sources and information there right now where a good descriptive study could be put together in a very, very short time, I'm talking several weeks, this information can be aggregated.

That might be helpful in determining as to where you need to go. More importantly, where you might not need to go.

Thank you.

COLONEL PHILLIPS: The discussions of the board a month ago and then again yesterday certainly talked about looking at the various factors that are potentially associated and in particular they're not always the ones

that make the front page headlines in the Washington Post and the New York Times. And, it may be that the board noted that the medical literature to date has not shown any causal association between suicide and mefloquine. Though it is suggested routinely in the...

PRESIDENT OSTROFF: Any other thoughts or comments. Dr. (inaudible)

DR. : I want to point out that our pharmacy policy and standard section under the (inaudible) is nearing completion of a descriptive study of mefloquine potential side effects in a retrospective cohort on our Somalian veterans, in essence they've looked at the medical records of a 1000 Somalian veterans and there would have been a fair bit of psychological morbidity during the deployment and certainly there has been after deployment and they've gone through every single encounter, medical encounter and coded don (sic) for ICD 10 codes and then they're trying to apply some

standard algorithms that I guess pharmacists use to try to attribute the side effects, whether they were likely due to the effect and if there is some objective way of doing this.

The data has all been coded and it is undergoing analysis even as we speak. So if you want to get sort of the inside track on that to sort to see some of the phenomenology and what some of the issues are I can put you in contact with...

COLONEL PHILLIPS: That's terrific. That's exactly what we were getting at in terms of what we need to do first. It sounds like you've got a jump on that already.

PRESIDENT OSTROFF: Thank you very much. I know that, as I said, we had a great deal of discussion about this and I think speaking for all of us we know what a difficult issue this is. Not only for you, but for all of us. And, how important it is that we protect the troops and one point that I would emphasize

is the issue of compliance that has really been an important one for us and I know when I look at issues related to malaria in general that the more flexibility that we have in terms of the options that are available, not only within the military, but outside of the military, for malaria chemoprophylaxis the better. And, I do have significant concerns that we have lose the option related to mefloquine because it does have some very valuable uses and I know that there is tremendous concern out there amongst the troops about this particular drug.

Most of the board members, at least with the presentations that we've heard up to this point, do not see a strong relationship between the suicide that have incurred and the use of this drug. Of course that's why it's so very important that we document this. But there's a tremendous image problem here not only with mefloquine but with doc compliance in general. And, that's why we feel it is very

important to see what we can do to help you to make sure to maximize compliance and maximize the (inaudible) we get for the troops to try to do the right thing.

DR. WINKENWERDER: Steve, I appreciate those comments and thank you again for the presentation. Let me just make a few remarks with respect to the issues that we face and at least how I view it. In trying to step back from all of the discussion and individual cases that have emerged or have been brought forth in the -- largely in the media, but that's sort of putting the question to me directly I felt that it was absolutely necessary that we do this study or these studies now that you've described them in the series, at least a couple or two or three studies.

So I'm glad to hear about this today and the progress. It's important. I, too would share the perspective that we don't want to take away any options that we have. And, so

I go into this with that as the thought in back of my mind.

On the other hand, as we look at what we're using today and across the world we have had certainly a case here, an incident that occurred in Liberia, just a few months ago where we had I believe over one hundred cases of malaria and darn near had two or three deaths. There were clearly some non-compliance issues and it wasn't because they were using something that they were supposed to be using, as I understand it, mefloquine.

I don't know if adverse attitudes now is believed or whatever entered into that equation or not, but when you talk about compliance, I think we have to look at both sides of it not compliance with something that may be quote "easier," to take, but also how people's belief systems in folks where they're willing to take things. And, there's a picture about compliance. I wanted to understand again

in terms of the descriptive studies imports, who's got the accountability for them?

COLONEL PHILLIPS: At this point in time the AFEB is going to have a written draft of -- a written copy of these recommendations that they will give to you and at that point in time then it becomes our health affairs responsibility again to initiate the studies based on the recommendations of the AFEB.

DR. WINKENWERDER: Okay, do you think we'll have these recommendations, I mean is there something we'll have like in a few days?

COLONEL PHILLIPS: A few days.

DR. WINKENWERDER: Because I am interested in tasking that out of course as quickly as possible which leads to my next comment is what do we think the time line time to complete the target date would be, at least for the descripted study? Sixty days, is that

something that's doable?

COLONEL PHILLIPS: A preliminary look is certainly doable within sixty days. If we start going out and looking for log books and medical record reviews from -- well, even for a really indepth comprehensive descriptive study it will take time to get people over there to look at that.

DR. WINKENWERDER: Because I'm interested as soon as possible, and again identifying who we're tagging with accountability and with a time line. That's my main two questions. Who's going to do this, when are they going to get it done? So I appreciate hearing about it. It sounds very good to me and it was good to hear about the other study result that may be available that would help with this. So to the members of the board we're pressing ahead. For whatever risk there may be, I underline may, we don't know that there is for use of mefloquine. We do have

far fewer people today on it than we did a year ago. It's not being used in OIF2 and I presume will not be in the subsequent rotations either.

PRESIDENT OSTROFF: All I can say is as long as there's a perception problem there definitely is a problem and whether or not these studies can be answered -- the concerns that are out there, hopefully there will be some way to (inaudible) and, we're certainly happy to help and be very enthusiastic in working with you and look forward to the designing phase and we will anticipate...

DR. WINKENWERDER: Great, and I have one last question. You mentioned non-DoD investigator corroboration, we have an idea who that might be. Would that be the CEC?

PRESIDENT OSTROFF: We'd be happy to do that, but I think that the idea was to in particular have a non-(inaudible)

DR. WINKENWERDER: And, in terms of the oversight, what was the non-DoD, what was

your thinking about that?

MEMBER: The DoD would be the same thing.

DR. WINKENWERDER: Well, I'd certainly concur with that and I was just wondering who it was.

DR. KILPATRICK: Dr. Fensom.

DR. FENSOM: Yes, thank you. Just for information for the board I recently also shared with the (inaudible) a policy that's addressed the issue of choice and we've instituted that early. Indicators are that troops, when given a choice in situations where there's no clear clinical advantage to one or the other that the majority are choosing methadone for obvious reasons and we'll have to be doing some work on how this policy translates to compliance (inaudible)

DR. PHILLIPS: The side effects is not going to be the way that the public looks at this and specifically the whole reason why we

got into this methadone study was in response to a lawsuit which was alleged that taking mefloquine in Somalia had a durable and permanent adverse mental health effect over the long term. So we had a very, very important group that shouldn't be missed.

PRESIDENT OSTROFF: And, that's part of rationale behind the (inaudible)

Well, thanks very much, why don't we go ahead and take a break and once again let me thank Dr. Winkenwerder for your interest and your support of the work that we do and all with the DoD.

Colonel Gibson has one brief comment before we break.

COLONEL GIBSON:

(speaking to audience about lunch)

(Whereupon, break was taken)

PRESIDENT OSTROFF: (audience noise) as is traditional we have a series of presentations. The first update will be from

Major Randy Smith and Major Smith is the preventive medicine staff officer from Joint Staff.

MAJOR SMITH: Good afternoon, ladies and gentlemen. My name's Randy Smith from J-4 Joint staff health service support team.

Today I would like to give a brief update to the board on several issues to include issues of concern to the battle commanders.

First I'd like to give an overview of the occupational and environmental health surveillance process. We'll discuss also some issues associated with that. Then I'd like to talk about first health protection countermeasures message that we recently sent out on how to improve some of the compliance-related issues. Briefly discuss the total force vaccination proposal. Then I would like to talk about combatant command issues of concern to the theater surgeons to include discussion of the

Japanese encephalitis issue.

PRESIDENT OSTROFF: Could you get closer to the mic.

MAJOR SMITH: I'll start with the occupational and environmental health surveillance process. The process can be broken down into four parts basically. It isn't just scaled to several policy documents and concepts of operation. Some of you may have seen similar information before, but in broad terms...

PRESIDENT OSTROFF: Let me just interrupt and say that he's doing Tab 13 in the middle.

MAJOR SMITH: The environmental surveillance health surveillance process can be broken into four phases; Phase 1, pre-deployment; Phase 2, immobilization; Phase 3, Conflict of deployment and approximately 30 days afterwards; and then the post-deployment which is primarily consisting of data reporting, archiving and surveillance.

There are goals in each of these processes. The first is to identify, assess and control exposures, occupation and environmental health risks; the first two phases a lot of that information is available at AFMIC, the Armed Forces Medical Intelligence Center now has an excellent database for occupational and environmental health hazards in many deployment locations and it's good for pre-deployment threat screening process.

Some of these sites can be eliminated during the clinical threat screen process during mobilization. In some sites you would never want to deploy to because of hazards to the environment.

During the deployment and conflict phase a document called the Environmental Baseline Survey, which has been recently renamed Environmental Health Site Assessment, they do conflict with several documents being produced by the line. This is used to generate a few of

the occupational and environmental health hazards at a given site.

Then finally we would archive would maintain the information for future deployments.

There's lots of guidance and policy on the occupational and environmental health surveillance process. Probably the key document is the DoD instruction 6490.3 which is currently undergoing revisions right now. And, will be available for staff. Some of you may already have seen it at this point.

Several other key documents include the joint chiefs of staff memo that are updating procedures for the deployment health surveillance readiness dated 1 February, '02. And, the JCS in improving occupational and environmental health surveillance reporting and archiving from 30, June '03.

Regarding records and archival accessibility the process can be summarized as

follows: The data's transmitted through the service of component channels and combatant commands through the Army Medical Surveillance Activity and information may come from several sources and many formats and data are used still exist in the field. Data from CHCS 2, Sams, Gems, whether it's Army, Navy or Air Force units will be sent to the JE system.

The JE system is currently being used in CENTCOM (sic) and in ACOM primarily and it's not currently connected with some other surveillance systems such as T-(inaudible) but that issue's being worked.

A new term solution is to transmit data through service channels and with copies being provided to health protection and readiness.

In summary, there are major efforts underway at the operational level to capture occupational and environmental health and medical surveillance data. As many examples

have been shown in earlier presentations there are still implementation issues for protective actions and medical surveillance.

In an attempt to clarify requirements and improve compliance the Joint Staffs sent a message to the Combatant commands and the services to try to provide clear guidance and improve compliance with establish policy. Some of the drivers of this policy were malaria outbreak at JTF Liberia which will probably be discussed in a little bit in more detail in a future presentation.

Some lessons learned from OIF and OVF and the potential for risk during (inaudible) operations helped motivate this. The key items include an emphasis on recording and transmitting vaccination status with service tracking systems are required to update VIRS at least weekly and many of them are doing it more frequently than that.

Use of bed nets and treated

uniforms are emphasized. There were some compliance issues like that associated with JTF Liberia. In deploying personnel with occupational health and safety protective equipment, this is not the same as MBC defense, IPE this has been a recurring problem in certain deployment settings.

Application of DEET repellents have been emphasized and proper filing and tracking and management of pre and post deployment surveillance forms.

A recommended practice in vaccination was developed by central command and is being considered as a model for use by other combatant commands and it has an electronic means to collect and maintain status immunizations and the service components, Army, Air, Navy, Marines, components would send their information and CENTCOM would track the information for vaccination status. An example of this is found on this website.

Switching focus I would like to briefly update the board on the total force vaccination proposal from the Joints of Staff and how it relates to the OSD vaccine program expansion package.

In response to previous discussions the Joint Staff submitted a proposal for a total force vaccination earlier this year in February and it recommends phased and prioritized plan to move toward Anthrax vaccination and acquiring sufficient smallpox vaccine total force vaccination.

This is designed to be a future way ahead complements vaccine program expansion package that the OSD has currently developed. It is not suppose to conflict with this. We are currently in coordination with the OSD offices and DEPSECDEF has additional input on this. We would also welcome any feedback from the board regarding total force vaccination proposals at this point.

Finally, I would like to update the board on some issues of concern of combatant commanders. This past January there was a combatant command surgeon's conference which brought together the surgeons general of the combatant commands and they brought up issues relative to them in their operational environment. I realize this is several months ago, but some of these issues continue for the combatant command surgeons.

Some of the key issues is clarification on vaccine program expansion requirements; request visibility on defense safety oversight council process and health surveillance metrics and access to those; concerns about TMIP fielding schedules. TMIP is theater medical information program and there are some concerns about the schedule of this fielding. Another concern by the combatant command surgeons was authorizations to treat other than U.S. Forces and some of this has been

rectified by recent policy decisions. Status report on investigation new drug requests. And, again this has been clarified by several recent policy decisions. And, the combatant command surgeons were also greatly interested in improving the interoperability and interchangeability of service medical assets. There will be another meeting June of this year, the second full week in June now at this point where we will address these issues.

Again, any feedback from the board, if you would like me to take anything back to the combatant command surgeons conference I can do that at this point.

An issue that I would like to bring up also will directly affect my combatant commands is the problem with the Japanese encephalitis program. The manufacturer of Beacon on discontinuing production in 2005. This may affect our Pacific command. Currently plans are to stockpile a 135,000 doses for use

by the Marine Corps in the Pacific theater.

This will approximately be about 18 months worth of usage with the current force structure and size. Beacon is developing a replacement vaccine but there is no plans at this time to seek U.S. licensure. We would like to request guidance and input from the AFEB members. Additional information is that there are two companies, Cambis and Vach(inaudible) that are planning on developing a vaccine projected for the 2006 - 2007 time frame.

And, several options that have been discussed which we request feedback on are, do we want to ask Beacon to pursue U.S. licensure; do we want to live with the existing stockpiles or develop a formal agreement with the Cambis and Vach (inaudible) products for use in the near future?

I will take any questions you have. Thank you for the opportunity to present.

PRESIDENT OSTROFF: Thanks very

much. You've obviously raised a number of intriguing issues that some of which I was not particularly aware of. Before we delve into the Japanese encephalitis issue which is an issue that's very concerning to me. Can you give us some concept or idea of what is the driver behind the desire to go full force protection for anthrax and smallpox because my recollection is that this was an issue that came up prior to Operation Iraqi Freedom and I know that in our previous recommendations regarding medical counter-measures we had strongly supported continuation of the current risk phase policy and part of our discussions previously was that obviously there is a long and difficult history with the anthrax vaccine and what got a lot of folks into a lot of trouble was the full force protection and there had been a current policy, from my perspective, seems to be working pretty well. So I guess I need a little bit of clarification as to why there is a desire to

potentially change that policy and the same (audience noise) smallpox and maybe you can help me with that.

MAJOR SMITH: Yes, sir, I'll try to do that. The Joint Chiefs, the chairmen's memo for total force vaccination was not considered to be a detailed specific plan similar to what OSD health affairs screening. There's a series of eight recommended courses of action to be accomplished in the near term, such as stockpile size and immunizing and immunizing different forces in different locations and this total force vaccination proposal was more of a long-term general request. The use of the reserves has been extensive in OIF and OEF and the Joint Chiefs office recommended that we consider a phase and prioritize a plan to move toward anthrax vaccination.

Regarding smallpox there was no plan or request to move toward smallpox vaccination. But they recommend acquiring

enough smallpox vaccines for this purpose for contingency.

In summary, the chairman's proposal was looking for a long-term way ahead while specific actions regarding numbers of vaccines and who exactly was vaccinated was more short-term. The chairman's proposal was more long-term. If the board does have concerns with that, then they can certainly re-address this point. I'll open it up to other members.

PRESIDENT OSTROFF: I'm fully supportive of making sure we have adequate supplies of these vaccines should we need to move towards more wide-scale vaccination.

I think that's a very prudent thing to do because if you don't know what the contingencies may require you to do things differently than they're currently doing them.

But that's very different than making policy change to what is currently being done. Do any of you others have any comments?

Dr. Gray?

DR. GRAY: I suspect a number of people on the board would be pleased to entertain a question regarding continuing the smallpox vaccination, that that would be helpful.

PRESIDENT OSTROFF: We don't need a question, because on an annual basis I have to make recommendations regarding this and so on the basis of the requirement the board make these recommendations we can add any suggestions we have regarding this -- recommendations.

DR. PARKINSON: Mike Parkinson. One thing that the board in particularly the (inaudible) (trouble with his microphone.) environment versus the service environment is the level of detail and insight that the JCS gets on the threat assessment. (inaudible)

So an issue of anthrax full force anthrax high risk I think that's for me is an issue. How much is the threat, how real is it

and how, you know (inaudible) a lot of people are exposed to anthrax. So I just don't know on what basis (inaudible) whether the most current threat we could get that would be more of a high risk in this country, so I think that's an issue that perhaps is the difference from a medical or public health standpoint (inaudible). The JCS level and the JCS surgeons, particularly when we still four years after (inaudible) we still have concerns about TEMA (sic) being deployed. We can't be saying that we're going to not do the right thing for vaccines because we have a hard way of tracking them.

If it's the right thing to do, it's the right thing to do based on the risk and the likelihood of that risk. (inaudible)

COL UNDERWOOD: (her microphone humming, staff trying to fix mic)

I just wanted to make mention of the individual readiness process with (inaudible) and I think this at least is a good

basis for looking at this longitude up and running forward.

DR. PHILLIPS: I can address your first question. Right now the threat assessments we're using that have been used are the same ones you were briefed yesterday on, the national intelligence estimate and the chairman's threat list.

There are no other assessments right now besides that. Now, central command has interpreted some of those briefings in relaying some of their threat information. And, it might be slightly more conservative but it isn't fundamentally different than what you've seen.

PRESIDENT OSTROFF: I will say I think that if we change our current policy we're just asking for trouble. Any way you can avoid trouble I think it's worth the wait.

DR. HERBOLD: John Herbold. I need some help in understanding the process.

We've seen a lot of process this year and I thought that if the Joint Chiefs said they need some protective measures for exposure to Japanese encephalitis wouldn't that be a kickback for some agency then to develop those protective measures and if that means a vaccination then that would show up on someone's priority list?

Can somebody clarify -- as I follow on this, are the Joint Chiefs or is there a mechanism to the Joint Chiefs as the combatant commanders to say, "we need access to the JE vaccine, period, and then all the other things work out."

PRESIDENT OSTROFF: Well, yes and no. I mean the realities of the situation and maybe I'll just sort of -- there are others more aware of this than I am. I actually did have some idealized -- clued into this particular problem a month or two ago when actually I had some discussions with a company. This is a

little bit more complex because while Beacon is the producer they sell this product through Aventis. And it's Aventis who is actually the distributor of this product. The one that sells this product in the United States.

And, the company is being required, the company that is the manufacturer is being required to change the vaccine, so the current vaccine dangers, is this (inaudible) the right vaccine, they are being required to sell (inaudible) product, and, of course, that will then have to go to -- if they go that route then they have to go through everything that's required for it to be licensed in the United States. And, the company suggested that they did not particularly see where it was advantageous to them to take the steps necessary to license this product.

In addition to that if they do take those steps there's an issue of Murphy's Law where things never go the way they anticipate

them going and so from my perspective, you know, hearing that there is a desire to have enough vaccine being in the freezer for an eighteen month supply is shortsighted in a number of ways.

One of them is that is based upon if you see something at the end of those eighteen months and the second is that if nothing happens in the part of the world where you use that vaccine.

That is a little bit different situation than adenovirus and we've been concerned enough about what happened with adenovirus. This one is a critical course protection measure if you have to go into certain parts of the world. And, so I don't think that this is a circumstance where somebody could get like caught with their pants down and not have the product when you need to have the product.

And, so I'm really, you know, very

concerned about this and we need to make sure in some way, shape or form that there is a licensed product that comes out of the end of this process and whether or not it's the product that Beacon is going to be producing or whether it's some other alternative that's out there I think somebody has to start planning now for what's going to happen, because otherwise we're going to end up in adenovirus 2.

DR. PHILLIPS: Steve Phillips. Sir, at the joint and policy group meeting last Thursday we had a conference call with the defense supply center in Philadelphia, DSET, who was ordering 135,000 doses for storage and my understanding the way the process has gone to this point is the (inaudible) first came about six months ago and we referred them out to PACOM, because that's where the vaccine's used in terms of determining what's the requirement for stockpiling long enough to cover the gap from the time they stop using the leishmaniasis

vaccine until another product is on line.

They're not pursuing the new Beacon product. Beacon has no intention of getting their license in the U.S. They're just going to let that market go. What they're pursuing is the VACGEN (sic) product and in our discussions with VACGEN we anticipate by '07 having licensed product available to sell to the United States Military.

Now, with that information they went to take out the requirements (inaudible) and the number 135,000 actually came from PACOM to the Joint Staffs to DSEP. Now, what DSEP has done is they've ordered 135,000 which will start getting delivered in I believe January of '05.

We've got until the end of -- September, October, the end of October to as much as double that order if we determine we need more than 135,000 we can go up to 270,000 doses. But Beacon has indicated that that's as much as they can produce. So the situation as

it stands now is that military is going to purchase a stockpile of the old vaccine which is anticipated to last until the new product comes out and I think it is the VACGEN is the one that's being pursued.

PRESIDENT OSTROFF: Well, I know that, you know, in the perfect world 2007 sounds great, but as we all know the world isn't perfect. I know I asked the question when I spoke to the company about the shelf life of the product and they indicated that it does have a relatively short shelf life, but there would never be a problem in terms of getting the shelf life extended, if that particular product in keeping it as an licensed product well beyond the approximately three years that it would be dated for use.

And, so I think it's really, really, really dicey to anticipate, to think that in 2007 there's going to be an alternately licensed product from another company. Because

it just never goes that way.

And, I would -- I mean I have no vested interest in this one way or the other, but I think that there are just too many variables here that could fall apart on this.

MR. HOKE: If I can just follow up on one other thing on that. My understanding is the way that the discussion went is it also involves who's going to assume the risk for the purchase and DSEP has assumed the risk of the purchase of 135,000. The other factor to consider is the preventive medicine community at PACOM was consulted specifically with regard to continue on the Korean (inaudible) and that sort of thing. And, those numbers -- but the requirements for the (inaudible) and they came up with that original 135.

If you go beyond 135,000 then the DSEP's going to say, "wait a minute, we don't have the money or they are going to go back to the Joint Staffs and say, "Okay, who's going to

kick in the money?"

PRESIDENT OSTROFF: I understand that. You can pay now or we can pay later. And, that's what we run with adenovirus. And, so, you know, they're being penny wise and dollar foolish.

DR. WILLIAMS: Greg Williams from the joint. Just sort of as information for the board this issue of Japanese enphalitis vaccine came across my desk maybe about eight weeks ago and just to give you a little information about what we've done over at the (inaudible) is I put Dr. Tom Monna, who's the project manager for CANVASS, he met the Navy Research folks down in Silver Springs and there is currently some discussion about cooperative research agreement for fielding the (inaudible) vaccine that CANVASS is they're ready to enter into their Phase 1 trial, the idea being that the epidemiological landscape has already been done by the Navy research group out in (inaudible)

and a canvass has already got enough vaccine for the the (inaudible) it's already been produced and set aside for testing.

So that's currently being worked out. In addition to that Dr. Wellington's group down at WRAIR is looking at working with the Marine Corps, I believe, in Hawaii to get a cohort approach to enter into Phase 1 (inaudible)

DR. KILPATRICK: My only comment about that would be that the ACAM 2000 would be Phase 3 trials. And, it's unknown when that's going to be licensed.

DR. WILLIAMS: I'm sorry, the current information I have from Dr. Monna is they are looking at 2007.

PRESIDENT OSTROFF: I can tell you problems happen. It's predictable that there will be problems.

DR. PHILLIPS: Well, I spoke to you earlier about adenovirus vaccine and those who

have been around a while will appreciate the irony of my making a comment about the Japanese Encephalitis vaccine, and you know, it really is, it's so adenovirus all over again that it's almost eerie. The DSEP waiting in, being the centranal that notices a problem, trying to handle it themselves like they did with the adenovirus vaccine, realizing it's much too complicated. They're great folks there for supplying vaccine to the military, but they're not going to be able to help a canvass of -- to get their product done.

I've asked myself, you know, how should we react? We've heard comments here about activities going on here and there between different groups of people. And, maybe as I've gotten older and life seems simpler to me, you know, what is right and wrong, but this is an example of an acquisition problem. We didn't have a sustainment plan for this vaccine or for any vaccine, for that matter. It's all kind of

reactive.

And, now we have a problem. And, we need to have a recommendation from the board, but the board doesn't set requirements. We don't have a requirement for the Japanese encephalitis vaccine. Now, there's probably an implicit requirement, because it's in the policy that certain people that receive Japanese enphalitis vaccine and that may be enough.

But basically someone's got to have an acquisition commission to get a new vaccine on board. And, in the larger context, to have a strategy to deal with Japanese encephalitis should there be a war in Asia. One thing that I learned in having these companies, having these companies that are calling around dutifully telling everybody just like Wyatt had the adenovirus vaccine.

This time it is good though, because the coin is dropping a little bit faster than it did before. The one thing I learned was

there never was a contingency plan for Japanese encephalitis. There's no vaccine. If we have a war in Asia there's no Japanese encephalitis vaccine for us. There never was. We have never had that capability.

So, the question is, you know, how to we -- and of course you know the board has been absolutely totally in the middle of this vaccine since World War II and all of that whole story. How does the DoD now take a big breath and say, you know, "where is the recommendation, where's the requirement, where's the palm, where's the plan, where's the solicitation, who's going to support the companies and make sure that this gets done."

The DoD can't just hope that some company steps up and does this for free. So hopefully we're learning a little bit on the adenovirus vaccine that can help us figure out a way to move forward on this thing. But I think the fact that you all are hearing about it today

is probably the most important thing that's happened.

PRESIDENT OSTROFF: I can use the blueprint that I have for the adenovirus letter.

DR. PARKINSON: One major difference is that this is a warfighters vaccine. We're hearing the presentation from JCS, we have got to find a way for JCS to basically say this is a wartime requirement and in my experience that goes right to that (inaudible) including the people here under the the two star and everybody in the requirements world saying, "this is real. In eighteen months we can't go to war in this theater," because the human weapons system will be unable to fight. Or we basically say, if we need any help from ASED, then we need to go right back to the chairman and say, "this is a real threat. It's a live threat to the performance enhancement and mission completion. And, we all could use the template (inaudible) with JCS generating a

requirement saying, "oh, we've got a yellow or a red flag here for liability, that would drive the system to come up with an actionable, accountable plan within eighteen months.

I mean, we don't have a single warfighting system where we say that's the sole way to fight the war to the backups to the backups to the backups. We need the same thing for a vaccine to prepare our troops.

COLONEL PHILLIPS: I'll take that back to my leadership, sir.

DR. FU: We've heard that the manufacturers plan to discontinue the production next year, is that correct? But how firm is that?

PRESIDENT OSTROFF: Well, now when they re-start production they're going to be making a different vaccine.

DR. FU: Oh, I see.

DR. PHILLIPS: It was presented that -- the option that DoD could just continue,

but it would cost a lot more, because there wouldn't be anybody else to share the basic cost.

PRESIDENT OSTROFF: They also said that DoD could pay for the trials to get this product licensed and my understanding is that DoD signed that particular option.

I have some difficulty reconciling this issue of total force protection for anthrax and smallpox and letting basically the ball drop with a mission critical vaccine like this when you know the disease is out there. I just don't understand it.

Any other comments? Thanks. I know you're just the messenger, I understand completely. Our next update is from the Army, it's Colonel Underwood and good to see you again.

COLONEL UNDERWOOD: Thank you. Switching topics here, I want to give you some updates here about Leishmaniasis. Well, this is

just a cartoon a tutorial of what the life cycle is with the sandfly. It's very small, it's about the third of a size of the mosquito. So a lot of people that get bitten actually don't even realize that they've been bit. But there's a life cycle in this case with a dog or other mammal, bites the dog, the dog gets infected by this cycle and it lands on the human being and injects Leishmania into the skin. That gets into the bloodstream and it causes cutaneous Leishmania or visceral leishmaniasis and then it continues with the cycle there as it bites another animal.

What we're experiencing in Iraq, this is a map that we were able to get from the equivalent of an Iraqi center for disease control. The date is 2002 and it gives a rendition of where they have most of their cases. This is cutaneous Leishmaniasis. If you look at the circles here these are the areas where we've experienced the greatest number of

cases in our patient interviews going back from May through October of last year.

Well, since January it says here 618 cases, in fact, I'm here to tell you that we update this weekly and our total as of last week is 635 cases of soldiers and U.S. Marines who have cutaneous Leishmaniasis and we've got 3 service members who have been diagnosed with visceral Leishmaniasis. I think back to the point at Fort Walton we hadn't gotten any by that point and now we have 3; 2 of them were from Afghanistan and what is more worrisome now is we have the first case of visceral Leishmaniasis coming out of Iraq.

Our main goal, of course, is to try to prevent this because it's really a top protection priority. So we want to put the emphasis on educating the soldier for some protective measures. And, to that effect we developed, I should say CHIPPM developed cards. Let me see if I can get it to that slide.

I placed some cards. For those of you in the back there's some cards on the table back there. Essentially CHIPPM produced two types of cards, what you're looking at here really is the DoD system of personal protection measures. This is the DoD insect repellent system, the smaller card with the circle in brown. And, the idea is to suppress the reservoir if we can. That doesn't work very well in Iraq or to suppress the vector.

I might say that in efforts to suppress the vector that was not very successful in Iraq, so what we really want to focus on is personal protective measures. These sandflies like to bite mainly at night. So at two o'clock in the morning when people are trying to sleep, if they can, without much clothing on, so they're got a lot of surface area there to bite. This is the real risk.

So what are we asking them to do? We're asking them to keep their sleeves down, to

keep their clothing on, to use an insect repellent with DEET and to treat their uniforms with Permethrin and to treat their bed nets with Permethrin.

Now, the other card you see is the first interaction of the Leishmaniasis card. That shows the picture of the sandfly, it shows some graphic representation of what cutaneous Leishmaniasis looks like. On back there you will see some contact information. I want to tell you, this was the first iteration. We really didn't want everybody calling Colonel Naomi Aaronson. She is the foremost authority in treatment for Leishmaniasis in the military and she's very, very busy.

The new card that CHIPPM is working on is going to list a 1-800 number for the deployment health clinical center at Walter Reed and there will be two numbers, one number for worried individuals, another number for providers. There's also a 1-800 number in

Europe and that's going to be on a new card.

Let me tell you that they worked very hard to distribute these cards so the first iteration these numbers refer to OIF 1 and you can see there that almost half a million cards to get out to the folks. Somewhat fewer percent of sandfly cards.

All right, so what are the products that we want them to use. Well, DEET, very important. We put both products there for you to see because unfortunately we also run into a perception problem as you well know, soliders are more likely to buy something that looks nice. It's exactly the same thing, but we run into the issue of something in OD green doesn't look as attractive, but it's the best product there is.

We also have IDA kits for treating uniforms with Permethrin. We also have the Permethrin aerosol spray cans. The surgeon general asked us about the availability of these

items. Why are we getting so many cases were these items available. So we started to look into that.

We did find some problems, but let me tell you what was available first and Permethrin, this was very recent, as of 1 May, you can see that we have sufficient supply of Permethrin in cans in theater to meet the demand. This is information coming out of the defense supply center, Philadelphia.

We also have sufficient supplies of DEET to meet the demand. But where we got into an issue was with bed netting. We had insufficient stock to meet the demand. When we found this out things started to happen in terms of trying to up that and going to the war supply.

The contractor added a new commercial source. So now we have more additional bed nets that are doing it. You can see the plan there to get more bed nets in

theater.

They negotiated additional deliveries of 30,000 per month from August to September and they're also receiving a purchase exemption for a quantity of 120,000 to a recent 30,000 per month.

Before I get on to the treatment centers let me just say that this issue has already been briefed to Dr. Winkenwerder and to our surgeon general, so we were well aware of that and logistics -- logistics stepped up to the plate to negotiate increased amounts of bed nets. If I could quote Major General Farmer on this, he didn't think that it was too outrageous to say that there is a whole spectrum of force health protection. That can be as much as using the ceramic plates in the vest to prevent someone from being killed. But it also includes the other spectrum going down to using things like bed nets and vaccines, all of those measures for health protection.

So it was no small item that we needed to insure that we give the soldiers what they needed to protect themselves.

Now, as far as treatment centers, most of the patients heretofore have gone to Walter Reed to be treated. That is if they needed treatment with Pentostam. Because we have several options here and you might ask, "How do you know who needs what?" Well, it's really about the size of the lesion and the number of lesions. And, I'm talking about cutaneous Leishmaniasis here. Visceral I'll get to in a minute, the more serious disease.

But the cutaneous Leishmaniasis we're really concerned about the number of lesions and where they are placed and how old they are. We certainly don't want to treat lesions that are already epithelialized. But for those who needed treatment they were sent to Walter Reed to be treated with Pentostam. Colonel Aaronson reduced the treatment from 20

days to 10 days, because it's not, as you can imagine, it's not a very comfortable drug to give. It's given IV. But now we have also expanded the sites where we treat the patients. Brooke Army Medical Center has come on board also being able to treat with Pentostam. I might add, I'm sure you're aware of this, but it is under an IND protocol and so it has all the parameters that have to be adhered to with that protocol.

We also have other treatment sites in Blanchville which is services at Fort Campbell where they are using ThermoMed which is a heat device which essentially heats up the lesion to over a 100 degrees Centigrade.

They've also had some use with Cryotherapy almost like a wart clinic, if you will, and they've also been effective in freezing some of these lesions.

I might add that some of these individuals really don't need treatment at all

and we know, at least what we understand of the processes that it is self-limiting. You may end up with a scar, but some people elect not to be treated and/or they don't come in for treatment.

What's the road ahead here? We've already taken some steps. This, I might add, of course we know that this is really a commander's program in terms of force health protection. We give the best medical advice that we can give. What we're looking for always is compliance and what the commanders have to do, and we need to help them, do is to take care of their soldiers.

One of the things we did is we had the surgeon general send memorandums to the 1st and the 5th Continental US Armies and reminded them about the use of personal protective equipment. We sent out an ALARACT, which is an all Army message on Leishmaniasis. We actually did that back in November and we're sending out another one on several issues, but leading on Leishmaniasis.

We also wrote a change in the personnel policy guidance. This can be found on the website, the G3 website. They've now changed it from calling it a PPG, they now call it Chapter 7 on medical and dental issues. But we wanted to put some emphasis in there about Leishmaniasis in particular.

We made a change in the deployment list. What do we mean by this? This is a DA 7425 which the commander has to sign off on this list of various items to insure that his and her soldiers have these items so we included the personal protective equipment on this list. And, of course, again we can never reiterate too much about command emphasis.

So in summary, obviously primary prevention is the best. We want to primarily prevent people from getting Leishmaniasis. We're coming in to the season now again, it goes along with the mosquito season, if you will, starts up in April, goes through probably the end of

September - October. It has a long incubation period. One thing that we're very concerned about are the cases of visceral Leishmaniasis because it may not appear for weeks or months later, perhaps even years later.

So we're in the process of getting a campaign together for civilian physicians, the surgeon general is going to give assistance through his public affairs office on this to get a letter out to civilian practitioners to look for this in people who have been released from active duty who may show up with fevers of unknown origin.

The secondary prevention involves methods and procedures for identification and treatment. And our current treatment options, again, Pentostam, ThermoMed, cryotherapy, fluconazole, I know this is actually off label, but they have found some treatment success in using fluconazole and if they get visceral Leishmaniasis, and material that really is

Amphotericin B.

That concludes my briefing. I'm ready to take your questions.

PRESIDENT OSTROFF: Thanks very much. Before we open it up let me ask one question. What do you know about the individual in Iraq that was identified as having visceral Leishmaniasis in terms of where he or she was deployed to and are we talking about a large number of other personnel that were essentially in the same location?

COLONEL UNDERWOOD: Well, what was so worrisome about this was, actually he was with the Second ACR, he traveled -- he had two weeks in Kuwait before he went into the country of Iraq and he essentially stayed within 50 miles of Baghdad. And, he worked as an escort gunner for very high people in high positions, including Mr. Brehmer.

So he does not remember, from the history, any bites. He does remember having a

few mosquito bites. He did not use DEET, he did not use Permethrin, he was in an air conditioned building. And, part of the dogma we know actually that as the fields mature or as the situation matures our dogma is that it's better to be in air conditioning buildings where you don't have to use bed nets, but this is very worrisome. But then, on the other hand, if he was just traveling around we just don't know where he was exposed. But the fact is that he was not far from Baghdad.

A concern is this is probably a tip of the iceberg. We will, of course history will tell us now what happens. If we compare this to Desert Storm I believe we only had 12 cases of visceral Leishmaniasis, someone can correct me if I'm wrong on that.

But in Desert Storm, unlike now, we weren't there for a prolonged period over the season where sandflies are actively biting. So this is the concern that some people may show up

weeks to months later and how are we going to address that and this is of concern.

We certainly need to educate our physicians out there that might potentially be seeing patients with visceral Leishmaniasis. I will tell you that one of the two cases of visceral Leishmaniasis of Afghanistan, actually they were about to treat him for Hodgin's Lymphoma before they thought about Leishmaniasis in the differential.

PRESIDENT OSTROFF: Col Hasselquist.

COL HASSELQUIST: Yes, sir. You just mentioned it briefly there, but what I was going to say one of the major engineering controls that you weren't mentioning in your slides was air conditioning. It's worked great for the Air Force. Unfortunately, one of our prevention slides is showing an Army unit where it was too hot in the tent and they were sleeping outside with their clothes off when

there's thousands of flies around. So I'm not sure what the Army is doing to get air conditioning out there sooner in their tents. But obviously engineering controls are working well but people don't wear DEET and don't go along with everything else.

COLONEL UNDERWOOD: Yes, that's very true. I think that you could say -- in some ways we don't train as we fight. In the very austere conditions before the infrastructure is really built up and before we can get air conditioned barracks or air conditioned buildings we need -- getting back to the command emphasis. As ugly and as difficult that is, because believe me I've been there I know how swelteringly hot it is. It's miserable.

But then this is what we see out of this. That we have so many cases of cutaneous Leishmaniasis and this is the results of that and we do know that the barrier methods

work. We saw this excellent presentation at Viewmet when they were talking about the malaria in Liberia and all the barriers that had to break down in order for them to get malaria. Not using the DEET, similar things, not taking their bed net. All of these things are available to prevent us being bitten and the results of that is we see these numbers of cases.

It will be interesting to know as the infrastructure matures to see how many will occur in OIF 2 and 3.

PRESIDENT OSTROFF: My only comment would be I hope that the average person that's going to Iraq has better eyesight than I do because...

COL UNDERWOOD: It's too small.

DR. CLINE: A couple of questions. I wonder for those who do not have the luxury of air conditioning what data do we have available on compliance with the various personal

protections including bed nets?

COLONEL UNDERWOOD: It's interesting that you ask that question because there was a small study done in theater by an entomologist working at compliance. I'm sorry to tell you it was really very pitifully low. It was on the order of 15 to 30% that these protective measures were...

DR. CLINE: I can imagine the enormous range of reactions to the risk and some people may say, "well, it's not that bad," or maybe they just put DEET on their face and their hands and say "I don't care if I get it elsewhere." I mean, we might go the whole range from DEET protection to nothing.

COLONEL UNDERWOOD: You know, I wanted to make a comment about that, because I don't know if Debbie Funk is still in the audience here. I know she was here yesterday from Army Times. A couple of weeks ago in Army Times she did several articles, one on depleted

uranium and one on leishmaniasis and she did hear of a very prominently, of a soldier with a very prominent lesion who was proud of it. In fact he said it's a badge of honor if you don't have this lesion. And, I thought, "well, thanks, Debbie, that's not the message we really wanted to get out there."

DR. CLINE: If we're going to be thinking about ordering an additional 120,000 bed nets I think we need to have better information about just how they will be used.

The other question I have is related to treatment. I mean the fact that five different treatment options are out there tells us that none of them are very good.

My question is, is there some comparative studies going on or are these just ad hoc some people do this and some people do that?

COLONEL UNDERWOOD: Colonel Aaronson is finishing up looking at her results

from the ThermaMed. She's also using ThermaMed at Walter Reed. And, she is finishing, but I think she enrolled about 50 patients or so in that particular study, so I can't steal her thunder in terms of what her results are. But, in fact, they've had to retreat 12 on Pentostam that had to be re-treated.

But for the most part they're doing well. That's in personal conversation with Colonel Aaronson on how they did. Now, what is of interest and perhaps someone from the MRMC community can help me with this. But there is a topical treatment that was developed with -- now, I'm going to blank on his name, yes, Max Grogle developed with many others a topical perinolmycin with, in fact, in his studies, and he studied that first in Brazil, but then changed to Colombia when they had a lot of cutaneous Leishmaniasis and from preliminary results the cosmetic result from that is really very fantastic and I understand, Dr. Hoke, that

he might have a commercial partner now, but I shouldn't say that, but at least it's on the horizon as another treatment option.

DR. HOKE: TEVA (sic) a generic pharmaceutical company in Israel markets a very similar product and I guess the question would be why not go to the similar one that's already marketed and licensed in Europe and try to get it licensed here. And, I just wanted to make a comment about licensed products. Pentostam has been on IV since 1979 in the Army and I don't know how long in the public health service.

This isn't really what the 21 CFR contends. And, we do not want the long term IND's. Lots of manpower has been expended filling out forms because this is a drug that's being used under IND . I personally think that licensure should be sought. Here are the reasons that I have been given why that isn't done. We don't have a budget. WAXSO (sic) doesn't want to do it. There's not enough

market.

It seems to me there's some good reasons to force licensure or get another company. For example, another reason is that the manufacturer is too unpredictable and the process isn't good enough that it can't be well enough to find chemicals. You hear all of these things as reasons why it can't be licensed.

Well, I'm kind of appalled that we continue to do this since 1979 and give this medicine to soldiers without going through the vigorous process of reviewing it for licensure. If it's not manufacturable, reproducibly, if the company isn't doing it right, if, you know, there are other issues we should correct it. We shouldn't be using it.

But to use it under IND is to assume all that responsibility ourselves. And, without the benefit of the FDA looking at it, so when I was head of the infectious disease program I said the only thing we really need for

cutaneous Leishmaniasis is a licensed treatment for cutaneous Leishmaniasis and if that's Pentostam fine, and maybe the other things. But look at all the machinations we go through, bring them to Walter Reed or to Brooke's to get this treatment. The only reason we took it to IND is because it's IND and that's where the protocol is.

So we're going to all this trouble to avoid the licensure question which personally I think is a mistake.

PRESIDENT OSTROFF: I'll just mention the person who's responsible for the infectious disease protocols for CDC we have about a dozen similar drugs that we have in certain products like this and all of them are like protocol No. 6 and protocol No. 7 and protocol No. 5 at 6000 already at this point.

And, we've had these products since well before my time at CDC and we have lots of them like this that. You know, some of

them we use one every five years for African (inaudible) or something like that and there's just no market.

DR. KILPATRICK: I just wanted to make a quick comment since you mentioned CDC's. MFWR graciously worked with Naomi Aaronson to get two reports on Leishmaniasis out. One of them very quickly recognized the problem and there was a follow up and it was very, very helpful. I commend the Army for doing what they've done to additionally warn or notify the private sector physicians about this. We have been working on it for some time, thanks to CDC.

PRESIDENT OSTROFF: The last comment, Kevin.

DR. PATRICK: I just wanted to expand on what's being done to get the private sector physicians up to speed on this.

Is there a systematic approach that's done based on where these people are deploying from and where they're going back?

Have they been given information themselves to carry and give to clinicians that they see?

COLONEL UNDERWOOD: Just to answer that, Colonel (inaudible) who is my boss, has drafted a letter from the Army Surgeon General to send out to clinicians. The question is how best to get to every clinician, whether through the state surgeons, that's just the issue and then with the public affairs to get as much information out there as possible both in the literature as well as brochures and publications.

DR. PATRICK: Having been involved in physician education for a period of time it would seem to me that it might be more perfect to do sort of a micro mass targeting strategy rather then attempt to reach all 300,000 physicians in the country who are engaged in primary care one way or another. I mean these people are coming from specific areas when

they're deployed, so focus approaches a particular locales may be a greater bank for the...

COLONEL UNDERWOOD: That's a good suggestion.

PRESIDENT OSTROFF: I think we're going to go ahead and move on to our next presentation and the next update is from the Navy and we have Captan Kilbane.

CAPT KILBANE: Thank you, Dr. Kilpatrick, Admiral Ostroff, I'm Ed Kilbane and as you can see I work at USMC and I would just like to give a brief update on some of the issues that we've been dealing with on the U.S. Navy and the U.S. Marine Corps immunization recommendations.

I'm very optimistic about this, because I think in talking to some of my Air Force colleagues they've kind of gone down the same road a few years ago. Maybe their road wasn't quite as long, but they dealt with some

of these issues and resolved them for themselves and we'll probably wind up in the same place, but we've got to go through the same journey, I think.

We're about to issue an immunization in the Navy. They're supposed to come out annually. They expire automatically, but as you can see our last one was in 1998, so we're a little overdue. Now, the 1998, note, it's not that bad. But we do have a few issues that we need to update.

And, actually the three topics that I'd like to cover here before you are listed up there. The first one prior immunization think we can resolve at least that our Hepatitis B immunization is going to be weeks to maybe months. And, the yellow fever risk assessment is probably going to take us about a year and I'll talk about each of those issues specifically.

The proof of prior immunization

questions came up because hearing from our recruit commands, this is their most frequent complaints from the recruits and the parents. We have a practice as recruit commands of just treating everyone pretty much the same and have them roll up their sleeves and just give them immunizations when, in fact, somehow separating the recruits from their records.

The motivation here from people, the medical people at the commands is that they want to save money, primarily, and not expose these trainees to more immunizations than they require. So our practice in the past has been essentially silent officially on whether we can accept proof of prior immunizations.

What I'm going to try to do in this next note is to put in a provision that says that we will accept some proof of prior immunization and when I say that, the problem is we don't get a definition of what adequate proof is. So in consulting the pink book, in years

gone by in previous editions the pink book from CDC has somewhat addressed that. But I think in addition have been more recent that's been dropped. It's been de-emphasized. I have a feeling and we tried to make some inquiries of people at the CDC. But I've got a feeling of what is going on here is that there's a more of an emphasis on using registries to document prior immunizations.

So the pink book is becoming silent on the written record, because it's kind of decreased in importance.

Unfortunately, for us it has popped up and we're going to see what we can do about it to satisfy or at least addressing some of these complaints that are coming.

So we have to define what an adequate record is going to be and if you look in the pink book there are some mentions of what that is. It has to be a medical record, it has to be written and it has to be dated.

There are other requirements that you can put in here like, you know, what the manufacturer was, what the lot number was, et cetera. But this looks like the minimum requirements that you can glean from the pink book. So we're probably going to do that which means no family Bible records, no sworn affidavits that it is. It'll have to be medical records of some sort.

Now, kind of related to that what happened was, and the way the context of this came up was for this Hepatitis B immunizations currently our practice has been that all new accessions are going to be immuned to Hepatitis B. What has happened with that is that the recruits at most of the recruit commands are just being immunized with Twinrix.

That was the context of coming up with why can't we just go with a record of prior immunizations for some of these things.

The other alternative, which I

think was settled on by the Air Force, was that you just do serology and that way you have proof, laboratory proof of immunization. You don't have to check the records, you don't have to worry about adequacy.

So the group down at Paris Island we talked with them and we've come up with a plan because they wanted to do -- they wanted to look at other alternatives, so I suggested that they do a survey of their recruits. Now, they already checked the serum for immunity against vericella. So I encouraged them to spend a little extra money to take a portion of their recruits that were already drawn the serum and checking for Hepatitis B. Commander (inaudible) helped me with this. We had a couple of different people do different modelings of the financial aspects of this.

And, independently approaching it from different directions we all came to the same conclusion, that if you can prove that 10%

of your population is immune to Hepatitis B you're probably going to save money by testing everyone rather than immunizing them.

Well, they did the survey at Paris Island 65% of the people were already immune. So there's a huge amount of money that can be saved.

The problem and the reason this is going to take weeks or months to fix, is that the money from the testing comes out of a different pot from the money that supplies the vaccine and we just have to bridge that gap. Overall we're going to save a lot of money, but we're going to have to convince someone to spend the money for the testing. That comes out of the hospital budget versus spending money for the immunization which comes out of the recruit command. So we just have to find the right people to get that bridge and transfer the money over.

The only thing that they want to

do is they weren't interested in Paris Island in checking, you know, if people had medical records, whether they actually were sero converted trying to check the accuracy of people's records and see which ones would be valid and which ones would be less reliable. But of course the sero survey is not totally reliable because we know some people just don't convert or don't convert after there three shot series.

So we're hoping to fix or at least have another approach to this problem. Oh, the other thing too is that we're trying to squeeze the recruit commands, we're trying to force them financially into testing or finding some other strategy rather than immunizing everyone by decreasing the amount of money that we give them for the vaccine. And, I mean economically and because we're economically rational what they've done is they're really beaten up the manufacturer and beaten down the price so

they've been very good at that, but they haven't quite flipped over to the behavior that we would prefer, but they're getting a really good deal from the manufacturers.

And, the final thing this -- when I walked into the job and I think I was there for two weeks and I turned to the people up in my office and I said, "You know, we just ought to go cold turkey and not immunize anybody against Yellow Fever. Tell me why I'm wrong?"

And, that caused a lot of consternation. And, there in the beginning of my tenure that was just a little too hard to do. So anyway what we did was I decided the Marines were just going to have to put them in a drawer and not deal with the Marine issue, because they're just too highly mobile, they can be deployed into an endemic area on short notice, on a very short notice. It would be hard to assess their risks.

It would be much easier, I think,

if we try to tackle the Navy personnel. Now, why do we immunize all of these people? When I walked into the job I inherited the historic policy, but not the historic rationale. You know, that's buried somewhere in the past. So it's a historic thing, probably goes back to the Spanish American War experience and World War II in the Pacific and when the U.S. Navy got holding stations all over the world and operated and visited in endemic areas.

Also there are some logistic challenges with that vaccine in supplying it and also you want to give it at least ten days before exposure. It's a very safe vaccine. I know there's been reports of some difficulties in the last couple of years with it, but it's really rather rare that you have any problems with it. And, the disease can be lethal, and we really don't have treatment for it is hemorrhagic fever.

So there is a lot of -- there are

a lot of forces at bear here that make that quick decision just to stop it a little bit more difficult. So what we're going to have to do is we're going to have to start from scratch and model this with the -- with what is our risk of exposures, what are the problems and try to justify this. That's why this is going to take probably a year for us to work through because we have a lot of other work to do too.

And, I'm hoping to do a thorough job. The challenges are, you know, we have ships, they've mobile and they might go into places on short notice in endemic regions. I also kind of the same problem you get with Japanese encephalitis vaccine, you know, if you look at the risk areas currently, you know, assessing the risk is going to be a moving target because in times of conflict your vector controls break down, population movements occur. So the risk is going to change. Like when you send people into the area.

So the mobility's going to be a problem. The other thing too is we have two strategic issues that have come up. Unlike in the Cold War when we had planned deployments. We had a blue water Navy, now we have more of a surge mentality where we have everyone ready to go right away. We don't want people to have short notice deployments. We want to minimize the last minute preparations that they have. Yellow fever vaccine is a vaccine you give every ten years and so it's easy to get that out of the way for surge operations.

Also, we don't operate, or at least the idea is we're not going to be operating so much in blue water anymore, we're going to be focused ashore. We're going to be more ground water.

So, therefore, we're going to be up in areas where it's more likely to get -- that our people be exposed. On the other hand, you have to step back and say, "you know we've

got crews sitting in nuclear ballistic missile submarines, you know, we don't have to worry about them getting Leishmaniasis. You don't have to worry about them getting yellow fever. Why are we bothering with this?" The problem is those people may have to spend their whole career in that submarine.

We look around for people we knew would never deploy on a ship or overseas. We found the, they were called civilians. And, it's the concept that everybody in uniform is going to be subject to exposure, we just have to get a handle on how -- what that risk is.

What we're going to do is, I've got, hopefully some extra manpower coming to do this. One of the current residents was involved in -- I believe he was the one involved in modeling some of the hepatitis vaccine policy unbeknownst to me, but he must be pretty smart because we both came to the same conclusion, so I think he may be coming to help with this

project. Also he's got some background in decision analysis, so we're looking forward to that. We hope to get that done while he's with us.

PRESIDENT OSTROFF: Thanks very much. Realistically unless that ground water is like in the middle of the Amazon, you know, I don't get it. And, I really applaud you for helping to rethink this policy. As you know, we made this recommendation to issue the multiple related vaccinations I do know it's 2004 and you know where most of your ships are going more than ten days in advance. And, I realize there's the occasional time that they may go someplace relatively unexpectedly, but the likelihood that they're going to encounter a massive outbreak of yellow fever that nobody knows about is infinitesimally small, and I will point out that one of those fatalities that we don't give the vaccine was an Air Force active duty person. So, you know, you're not talking

zero risk here.

And, I just don't think it's appropriate to give vaccines to people who don't need them. And, so I applaud you for doing what I consider to be the right thing. I'll open it up for other comments.

CAPT KILBANE: In response to that, I don't know where we're going to come out. I mean we may wind up in the same place we started, so I'm not going to prejudge it, but I think it deserves a thorough look from what the assumptions are. I can't find the original ones that led to the policy we've got right now.

PRESIDENT OSTROFF: Because it's probably not written on paper.

MR. GAYDOS: Joel Gaydos. Did you say that 65% of the Marine recruits had antibody Hepatitis B?

CAPT KILBANE: Yes.

MR. GAYDOS: Well, that's very surprising. There was a study done by Dave

Trump and some other people from uniform services that was a cost-effective analysis and it was done about two years ago and they concluded that if the prevalence of antibody was greater than 12% then screening was the way to go and the Air Force conducted its own study recruits and the Armed Forces Medical Standard people at Walter Reed took 2001 sera from the serum bank, the Army/Navy serum bank, about 2400 people and the test was the OSA (sic) test that was done by the Air Force at Brooke and they came up with the Marines, the Navy and the Air Force recruits and overall prevalence of about 29.29%. I think it was about 27% for the Marines, 29% for the Navy and about 31% for the Army.

I don't remember what the Air Force separate study found, but their percentage was about in the same ball park, so I think this is quite different if you would come up with more than twice what the other people found.

CAPT KILBANE: Well, you know, I think if you look at the competence intervals, I mean I think you could go 15% on either side of that, because of the study side, so maybe it's 50%, maybe it's 49%.

On the other hand, too, you want to talk about limitations in the studies, this was done in the springtime at this recruit command. Their population varies during the year, you know, during the fall they get the high school graduates; during the wintertime they get a slightly more mature group in there, but then you would expect maybe they wouldn't have been in the catch up, you know, that was recommended for adolescents. So you can argue one way or another. But it is over 12%, there's no doubt about it.

DR. HOKE: What we're dealing with here really is a continuing issue. We saw this back with polio. About 25 years ago somebody said, "well, we're immunizing everybody against

polio so the military can drop polio." And, we did a serum survey about late '70's we found out that that was not what we were seeing when we were doing the sero survey.

With regard to Hepatitis B, assuming that we get very good coverage in civilian population, I think from our perspective in the military questions would be how fast is this coverage appearing in our military populations.

And, then the other thing is, is the persistence of immunity and I think it relates to how often we need to be monitoring what we're relying on seeing on the civilian population with regard to the antibody prevalence or immunity from immunizations.

MR. HOKE: Well, the normal is not immediately immunization. It's how to figure out how to effectively immunize those who are going to need it. But it's a strategy.

CAPT KILBANE: But if we do that

now it may not be valid two years from now, three years from now. And, in fact, it would be very interesting that if in the three year period that we're looking at from the time the studies were done, but I just mentioned in your study if, in fact, there has been a dramatic change in what is happening with regard to the incoming trainees.

PRESIDENT OSTROFF: Dr. Patrick.

DR. PATRICK: Joel, I wouldn't be surprised if there may be a real object, because we have a lot of these universal adolescents is hitting this generation. What I wonder is on this issue of immunization registry passage of information into feeding in to this system is there any conscious effort to link the group of entities engaged in immunization registry development with what your needs are? And, let me step back and think again. When people leave high school, leave sort of K through 12 and they go into college or they go into the military and

some go into the work force, I know I spent a big part of my life in college and it's also equally important in college settings to know the immunization levels are appropriately high level. What I don't know is if you are engaged or DoD is engaged in with the CDC...

CAPT KILBANE: Yes, Commander (inaudible) created that, correct me if I'm wrong, but my impression with the interaction we had with CDC was that's the direction that the world is going towards.

But it's not quite well-developed enough to be, you know, reliable enough or encompassing enough to be integrated in to any comprehensive system yet and it may be quite a way down the road.

I mean it didn't answer our immediate problem. If there were a lot of those registries out there, if they were all pretty much connected together, then, you know, hooking up with them would have been, you know, that was

obviously my first thought, you know. That there's a database out there, let's go at it, because the cost to getting that information is very low. But it wasn't there.

CAPT KILBANE: I'm not surprised that that's the answer, but again having been involved almost ten years ago now in San Diego county's (inaudible) efforts to developing an (inaudible) registry and seeing it grow and seeing its movement grow now's the time to really begin to begin to lay the groundwork. And, I think this is a wonderful opportunity to potential engage in and to see the persons at CDC with representatives from the military and eventually other stake holders in setting up what five to ten years from now could well be what it is we want to have. Because again remember the landscape of vaccines is so dynamic that we can't think now, we've got to be thinking about what this will be to the 2B system that we have, so I think this is an

opportunity for us to -- I'm doing a little bit of work with NIP and there's an opportunity to find ways in which the AFEB could make recommendations that DoD work with NIP and others to make this happen in some way, so it might help.

PRESIDENT OSTROFF: Thank you very much.

(Whereupon, brief recess was taken.)

(back on record)

CDR MCMILLIAN: I'm going to talk real quickly about eye protection that we are working towards and also look at some injury patterns and leishmaniasis and we have slides on those to look at later.

We've seen some increasing eye injuries and we see an example here that eye protection can be very effective and we have run into some issues of style versus effectiveness. My next slide will show that in a little bit of detail. But the current goggle is very

effective. It's a fairly large coverage, it may be a little warmer in an environment because it's included around the edges. (inaudible)is the style, however, the new glasses with the wraparound and the brands with brand names seem to be more desirable and so the Marine Corps have done a large scale purchase. But a couple of different ones of these they've done some kind of in field analysis to see how that worked out.

Here we see demonstrated the concept if we had a helmet protector and you have the eye protector on. So what we're finding out in our injury patterns that we've been tracking is that the body armor is protecting the torso. We do have some neck protectors that we'll show you on another one in a minute here.

So the question has been when we're kind of looking at injury patterns and looking at what we need to do better as far as

protection. Just some quick stuff as far as the old (inaudible) burn rules that remind what the body size areas we're talking about. These are just raw data as far as injuries to parts of the body.

Down here in the corner where it talks about different patterns IED, that's your basic homemade bomb. IDF is your indirect fire. Mortars, artillery, things that are kind of lobbed in. Direct fire is guns that are fired. I'm not sure why they separated that as ambush and other shrapnel which would actually be more related to indirect fire and stuff and those are issues as far as data collecting that we've been working on trying to get that collected out.

But when we go to the next slide here we'll see that this is kind of down in percentages and if you go through kind of quickly you'll see things like legs and we're seeing a fairly high number, and then you take it down to even bigger, larger groups, notice in

the torso we're only seeing 10% of our injuries there. So we're pretty happy with the fact that the body armor appears to be working. But for the head and neck, considering that you've got a helmet on it's protecting some part of that, we're seeing a lot of injuries there.

Of course upper extremities and lower extremities that aren't protected it's not surprising that we're seeing injuries there. So far the upper extremity stuff, even in vehicles, the guys put their arms up can sustain upper extremity injuries while being in some degree of protection.

And, of course if you add all those numbers up it's about 384 total wounds in there. When you look at the killed in action, if you add these numbers up here we only get about 48 injuries out of a total of 50 overall and that mentions down here some of the massive injuries due to the nearby explosions and stuff are not included, because it's difficult to tell

what was exactly the (inaudible)

But these are spread out a little more and I think the wounded in action stuff is going to give us our better key. So because some of the chest injuries we saw are related to axillary and injuries along the side of the chest wall, we're looking at bolstering the protection provided to the shoulder area and along the side of the chest wall and this is kind of prototype stuff. You know we can wrap you up enough armor protection to avoid injury. Of course it enhances the axillary and the lateral chest protection, enhanced groin and thigh protection. We're also going to get a lot of enhanced perspiration and heat related problems with that.

So this is, of course, some of the stuff we're looking at. This kind of shows the neck protector, essentially what we've got in the field, but they're uncomfortable they rub on the neck, they interfere with the helmet use and

stuff. So we're looking at this as to where we're trying to go.

A quick look at Leishmaniasis. We had a fairly low number of cases for the number of people deployed to OIF 1. Currently we do have bed nets available. I talked about the next generation bed net when we did the malaria briefing the last meeting. The 1st of June they're going to go out on contracts on that so they're between the devil and the details of the logistic contracts and the EPA certification. So it looks like we may be able to get some stuff rolling on that.

Then on the next two items, the commercial Permethrin treatment and factory-treated uniforms we do have one company that's EPA certified and has a proprietary treatment method that the USDA has been testing on behalf of the Marine Corps.

Their testing involves actually putting it into a bug box looking at knockdown

over periods of time. Continuing to wash the clothing, put it back in to see what the knockdown rates are and then do GC's testing of the cloth material to see what the permit in levels are. This commercial product is up to 50 washings now and still getting knockdown ranges.

When they looked at the IDA kit, which is considered to be the gold standard for how we can treat stuff to be considered to be a lifetime treatment by having a new protocol it's only showing 5 washings as being the time that it lost it's knockdown capabilities, so it turns out that the Armed Forces Management Board (inaudible) the testing protocol and right now they're going to be revising how they're going to test Permethrin treatment to help account for this stuff.

So anyways, a new factory-treated uniforms, it turns out that the United States Marine Corps total contract for uniforms is coming up for renewal at the end of this year.

The primary thing we're trying to do is just add permethrin treatment as part of the standard of uniforms. So there are not going to be an untreated uniform available. The worst case we'll have to sign new SNS's for all of these and run them through, but that right now is the strong driving force to basically have a permethrin treated uniform as the only uniform available for replacement or for new acquisition.

Finally, just as a risk communication example of what we're seeing in the field. This is a poster that they're using for the Marines. They printed this up and they've got it posted all around and they found that the little picture of DEET wasn't doing too much and the sandfly is really not that scary looking and the guy with all the bug bite isn't to impressive, but the little baby with the lesion is really getting their attention and so right now at least they're are reports in the

field that the Marines are doing a pretty good job of complying with their protective...

That's all I have.

PRESIDENT OSTROFF: Thanks very much. Let me see if there are questions from the board. First Dr. LeMasters and then Dr. Baker.

DR. LEMASTERS: You've given the results on the injuries to the arms and the legs. I'm wondering if you broke that down any further in injury by upper, lower, elbow (inaudible) and really localize where the injuries were occurring and did that really help you think about intervention in that area of need versus just the (inaudible) have you done it by joint area, that is one of my comments and then the other thing this neck protection that you were showing on uniforms. I thought football players have it on the back of their helmet. Couldn't you -- have you thought about putting something on the back of their helmet?

CDR MCMILLIAN: The ones for the football players I think are made for hyper extension prevention and this is really a ballistic shield to avoid something from penetrating the neck.

DR. LEMASTERS: I would think, you know, you could do a little Darth Vadar.

CDR MCMILLIAN: The question is do you want to hang a weight on the head or do you want to put it on the body. I mean there's all sorts of pros and cons for all this stuff. It just turns out that they have a couple snaps, on the current one, they can it. Of course they're working toward a lighter weight and more flexibility. Just last week I was in (inaudible) in fact, they showed us a piece of about a one by one foot square piece of material, but it's the second largest piece in the world right now, it's a new product they're trying to get somebody to manufacture outside of the lab environment that they're hoping will be

about half the weight are the current the vest and stuff, without the plates the vests are already about pounds. It's very hot and very stiff and very uncomfortable. The neck protection the same thing. You know, it rubs and...

One of the comments on the helmet was, one of the problems was the weight so, they have reduced the weight by almost half, but now we are looking at more things like (inaudible) so I think alot of it was, we're trying to get away from hanging anymore weight on the head.

But as far as the other thing this data is coming just off our casualty reports and of course a lot of the stuff, like at the legs they don't get into thigh and legs. It's because a lot of these injuries are in multiple regions in the lower leg and a lot of these are injuries to both arms and legs and stuff.

How many of these, we don't have the data and a nice spreadsheet to say how many

of these are related to a trip fall during a battle versus due to actual impact. So it's kind of a rough battle...

DR. LEMASTERS: Yeah, but the injuries with the knee injuries, extra knee padding would be put into the informs and I imagine a lot of those groin, legs, arms, knees (inaudible)

CDR MCMILLIAN: This is a start. This is actually one and a half months into it. This is the second report that we've got, so we're okay right now. We're going back -- we don't even know yet what protective equipment they were wearing when this happened. So to try to correlate an injury with protective equipment that either worked or failed, whatever, we're trying to deal with that. There's no real requirement for this. This is just something they're looking at and they're going to pass it on to us and so we can pass it on to here. But this is -- we -- have a good system, and it's

good to see that they're actively collecting them like this and if we can get a little more information.

DR. BAKER: Sue Baker. Thank you for the information on the battle injuries and I'd like to hope that all of the services might be able to present the information on battle injuries and on-battle injuries. It can have tremendous effects on force readiness. I saw data from the Gulf War showing all of the ankle injuries that were occurring in volleyball and basketball when people were playing on rough surfaces and landing on stones and so on. This is not just a behavioral problem it's an environmental problem and if that's continuing to be a problem now in Iraq we can be skipping over playing surfaces, for example, it may sound silly in wartime, but this is what is putting people on helicopters to be evacuated and an ankle broken on the volleyball court is going to get an evacuation just as quickly as a shooting

of the leg.

CDR MCMILLIAN: Yes, ma'am. We do track the non-combat injuries...

DR. BAKER: It would be interesting to see some data on that.

DR. SHAMOO: I have a general question and it may reflect my lack of knowledge. As an adjunct when we know that troops are stationed, especially like in Iraq, why -- I haven't heard at all about what are the public health measures for sedentary work, or spray the trees or the flies or other insect biting, animals, I haven't heard at all talk about medications. Is that reasonable especially when we have stationary, we have places in Iraq where the troops are stationary.

CDR MCMILLIAN: I can add a little bit to that at the beginning but maybe Bill can answer that.

When we first looked at this (inaudible) was one of our locations where we

were having a lot of problems on it. The swamps had been drained there, the cracks in the ground, the sandflies were in the ground, aerial spraying into that area. It evaporated up, blew off and the same problem occurred on the site. So it didn't have a lot of impact from environmental spraying during this last part of the process. Bill may have more information. That's what I know from an additional startup on the problems with it, environmental controls just didn't work very well.

DR. SHAMOO: I mean, if it doesn't work is that an accepted? Have the people thought about it, planned a different protocol, or oil based, I mean I don't know. Even the sand, for example, I remember when I was a kid was sprayed sometimes.

MR. COURTNEY: This is Bill Courtney, I've never needed a microphone. All I can say is, yeah, we have at least one officer and four enlisted people plus a (inaudible)

hygienist at every base eyeballing this. You're not getting the nuts and bolts of it, you're kind of getting an overview of it.

As far as destroying all the sandflies, a lot of that was -- we could use DET maybe, but it's more of a beat them down if you can. We're going to try to change the environment there back to what it was before Sadam Hussein trashed it, maybe that will help too, but spraying just didn't work very well.

PRESIDENT OSTROFF: Can I ask just one question about the body armor? I mean again it's you know, as an infectious disease person it's not my area of expertise, but I know we talked alot about compliance related to some of the prophylactics.

What's the compliance like with using this body armor? It strikes me in the middle of summer when it's 125 degrees that's got to be really, really hot and unpleasant. I mean, are they -- do we have some data of how it

is being used?

MR. COURTNEY: It's tough to see DEET and malaria compliance at a distance, but body armor shows up and has protection really well. But that's really I think the basic answer is that things that are easy to verified are easily enforced. And so the guys are pretty good about wearing the body armor. I think the immediacy of the threat is again a big issue. They're heard about it or known somebody that was injured and anything that can protect them is something that they are willing to do. If you look at just the pictures in the press the guys are pretty good about wearing their equipment.

CDR MCMILLIAN: The other part is that they train with that, it's part of their basic battle gear and going out with -- I mean, they pump that stuff forever just because that is what they need to do.

DR. PARKINSON: Mike Parkinson.

One quick comment. We've gone through the notion that permethrin treated uniforms is pretty much (inaudible) but moving more in a formal policy way, maybe some of the other services can say this, to what makes sense to me is make it automatic that it just comes out of the factory for everybody, that immediately puts you in the threshold though of an imposed risk that hopefully we have understood any and all potentials about miscommunication or I didn't go for that. And, as you move forward on that policy just all of us have been there, done that and that is a step up on getting to the extent that we know it's a potential yellow flag as far as miscommunication and misperception.

PRESIDENT OSTROFF: Thank you very much. Let's take a five minute break and come back.

(Whereupon, off the record)

(Whereupon, back on the record)

PRESIDENT OSTROFF: Okay, our next

presentation is Lieutenant Colonel Bill Courtney, who's chief of the military public health. He is from the Air Force surgeon General's office and he is substituting for Colonel Woodward.

LIEUTENANT COLONEL COURTNEY: Thank you. Like I said I've never needed a microphone before, but I will speak into this so we can record. By the way I need to know the histrionics of these podiums. I had to bring my own adjuster.

Let me give you a real quick and dirty rundown on an issue that we've been wrestling with and kind of chewing on since we automated our immunization program. It may seem unimportant, it may seem a little academic to you out here and maybe at our level of headquarters, but it's something that really, really affects the bases, which I can explain a little bit later.

But I'm very happy for the

opportunity to bring this by this board. And, specifically we're looking for proper windows for some of our -- proper windows, grace periods, for some of our initial series and some of our booster vaccines. And, here's a quick list of the topics, but as background I think our ability to track immunizations to the inth degree kind of created somewhat of a dilemma. It really was never a problem back in the good ole days when we tracked immunization, basically I'd give them their yellow shot record and say, "you're going to be due in ten years, goodbye," maybe I kept it on a green log book, maybe I kept it on a home base, homemade spreadsheet or an a program that we created ourselves. We really didn't worry about it.

For the most part we found out people were overdue on the shot, we called them, "hey, you've been overdue for three years, let's give you a shot, or you're due in a month." It really was not a problem.

Now that we can give real time feedback on everyone's immunization status I think that has kind of created a little bit of problem.

Also we've really gotten our commanders, our line commanders attention on the importance of keeping up to date on immunizations; not only because they really realize it's important to have somebody immune when they're deployed, we've gotten their attention on that one, but also we're tracking these things to the inth degree, so the day after you're due from the AFCITA or whatever the package insert says the day after now you're not medically ready. You're overdue, you're a red mark and we're showing these statistics to the group commanders, to the NASA COMS and all the way up to the top and I can tell you something, our commanders hate to see red.

Especially when their numbers are being shown against other squadrons, other wings

and all the way out. So we've gotten their attention also for the good and also for the bad and sometimes that can drive some behaviors.

Commanders will say, "if you're going to be due on Sunday I don't want you to be a red tick on Monday, so go on and get it on Friday. If you're going on vacation for a month and you're going to be overdue shot, go on and get it, because I don't want you to be non-medically ready."

So perhaps we'll have created some of that to where the metric and the system itself is driving the program not so much the immune status of our troops.

We'll create a little breathing room, some yellow periods. It's okay to give a shot maybe a little bit early or maybe a little bit late. Because we don't know where there are some instances where it's a good idea to give a shot a little bit early. If our troops are going to be overdue while they're going to be

deployed, our recommendation is go ahead and give it.

Some rules right out of what Major Lynn got out of the pink book. It's not an issue after you finish the series if the periods were lengthened a little bit. Those do happen, I mean people have fevers and things where it's okay sometimes delay them, however we all agree we're not going to consciously decrease the interval between them. We're not going to consciously decrease intervals for some of these initial series of vaccinations.

How do we apply some of these rules to give standardized guidance not only for the systems, to build in our computer systems, we also give -- commanders ask us these questions. I think we have a relative large number of inexperienced providers, they do ask these questions all the time, "is it okay to give a shot early?" I think it's well within a physician's purview to give this sort of off

label, but they do ask us these questions all the time. A lot of people say, "okay, where's the policy of that stuff?" An example might be tetanus. Right now it's a tetanus shot every ten years or so except for if you step on the proverbial rusty nail, then it's within five.

You can argue that that's clinical treatment not real true prophylactics, but again it gets back to the issue what can we do for some of these other shots.

We want to inform people, give them an opportunity of when they're going to be due or maybe a little bit after they're a little bit overdue.

Now, along with every other service the Air Force policy is to require immunizations in AFCITA and keep current and see if somebody asked what that stood for yesterday when I was standing out there.

We have one yellow period already automatically built into AFCITA, that's

Hepatitis A where the recommendation is you give the first shot and then the second shot you give six to twelve months later. We've already built that into as a yellow period.

For the rest of them, like I mentioned, you're due the day after, if it's been ten years since your last one it's ten years and one day you're red, you're overdue. Again that gets rolled into an (inaudible) score, it's shown to headquarters, it's shown all the way up.

So what we're suggesting is to go with the ACIP recommended for the initial series here, plus a grace period of about a month.

So for Hepatitis B your second shot's due a month after the first one. We'll give you a grace period for one month after that.

The third shot's due five months after the second shot. We'll give you a grace period of yellow for another month after that

and you can see.

Now, when we say "yellow" that's going to show yellow in the local CETA, but when it gets rolled up to gets rolled up to headquarters we're going to make that green.

Influenza, I don't know if the other services is doing this, but on January 2 if you haven't gotten any you're going to be ready, period. So you wake up on New Year's Day there's a red mark and your commander with a hangover go forth...

For boosters, we're going to -- the recommended we're going to give them the ACIP recommended booster plus or minus three months. The three months really we pulled that, I pulled that because that's the average time for an Air Force, for the AF concept and Air Force deployment. So we give them three months in advance to say "go ahead and get the shots so you don't come overdue while you're deployed," or if somebody gets deployed and didn't get the

shot we can give it to them when they get back. I don't know that there's any really psych behind that, but I know this isn't acceptable.

Getting back to, this really for the vast majority of the Air Force is really for tetanus, because for the most part the Average Joe walking along the street on an Air Force base is not required to meningitis or typhoid or yellow fever.

What we're looking to do is adopt these yellow periods. If we increase the opportunity to give people shots I think this should give us some good guidance to give to our providers. I think our troops would be scientifically protected. It would give us more breathing room for the zealous commanders who hate to see red. And, it's not going to sap the base level troops that believe me being at base level for many, many years when you work hard, there's a lot of angst that goes on about showing red to the commanders when maybe we

don't need to.

Any thoughts on this sister service contracts?

PRESIDENT OSTROFF: Thank you very much. Any comments or questions? All I'll say is it makes a lot of sense to me to get people vaccinated.

COL UNDERWOOD: This is Colonel Underwood. In terms of where we're going with individual medical readiness we've talked about a grace period as well.

I think -- I don't know if there are any dentists in the room, but I think even we can take a lesson from the dental command, because I believe they allow one month grace period on their yearly dentals as well.

DR. HAYWOOD: I should have announced this question earlier, but we've been hearing a lot about vaccinations, immunizations, et cetera, but what about the heat problem in Iraq is that interfering with the troop

readiness and...

LIEUTENANT COLONEL COURTNEY: You mean heat stress, no, you know, I kind of worked at the Gen Center for a while but I don't know that that's a real major issue.

I think they get a pretty good idea that when you hit the ground in Iraq it's going to be hot.

COLONEL UNDERWOOD: This is Colonel Underwood. Yes, heat is a very big concern. We have had heat casualties. In fact during OIS 1 we had six heat-related deaths. And, we've had a number of heat strokes and evacuations for heat-related issues. Every year we've put out a policy on heat and the planned dose for water intake and preventive measures. But, yes, you're quite right, it's a very big concern.

LIEUTENANT COL: We spent quite a bit of time and effort getting the commanders and the supervisors -- that's who we concentrate

on, is the commanders and supervisors say, "drink water before you're thirsty." I've been through this drill a hundred times as far as briefing people. It is a huge problem like it was, no.. It is something that we're constantly aware of.

MEMBER: Do you think it would be useful to have a formal report on that...

PRESIDENT OSTROFF: I was going to say as well. Unfortunately it would be probably a little more ideal to have it at the PIP (sic) meetings since we're getting into the summer months. But possibly at the fall meeting in September we could get an update or presentation about the experience with heat-related problems associated with OIS?

LIEUTENANT COLONEL COURTNEY: That's a reportable, that's reportable now.

DR. HOPPER: In terms of -- could we have a view then of combat, the numbers combat motor vehicle, heat, sort of an overview

of the surveillance data.

PRESIDENT OSTROFF: At our previous board meeting we did have a comprehensive presentation on fatalities.

Now, at the last meeting we did raise the issue that fatalities are only one aspect of what's going on in the deployment and we did request trying to get some sort of an overview of non-fatal patterns of illness and injury and unfortunately, this particular meeting, because of the nature of this meeting and the fact that we have to classify and things like that it's difficult to try to work that into this meeting, but as we discussed at our break out yesterday afternoon, it would be, you know, helpful to have a different flavor to some of these as we move towards (inaudible) and I do think that we would like hearing about some of these other bigger pictures issues.

COLONEL GIBSON: This is Colonel Gibson. That's on my plans for the agenda for

the next meeting, it already was, because we picked it up from the previous one, but I just couldn't fit it in to this one. Dr. Courtney, I just have one question for you. You talked about when this rolls up to headquarters level your yellows would be greens, how long do you think that will last before it becomes yellow as well? Do the yellows stay yellow at headquarters? I've been down this road before as you have and I've seen a sort of mission creeps to identify yellows and reds?

DR. COURTNEY: We already have a yellow period on the metric right now and if you're below 75% you're yellow, if you're above 75 you're green. But I don't know how we could make that a different shade of yellow. I think it's -- when they roll it up if they're still within the window they're still green, they're still okay. They're 100% medically ready to deploy they just have to take care of that shot when they got a month to go.

PRESIDENT OSTROFF: Thanks very much. Our next update is from Captain Obrams from the Coast Guard.

CAPTAIN OBRAMS: Good afternoon. I'm here presenting for Commander Rodrique. She sends her greetings. She is not able to be here. I can't say that she probably is sorry to not be here, because she's (inaudible)

We have not heard from her, but we've been keeping our fingers crossed.

What I'm going to present to you is a little story and the lessons that we've learned from this story. The story started about two months ago when one early Monday morning our preventive medicine unit had a voice mail message that said, "A dog was taken aboard a Coast Guard cutter somewhere off South America. The dog bit 20 people, then died suddenly. The crew then threw the carcass overboard." Our preventive medicine group investigated. They questioned everyone they

could find.

The cutter had interdicted a Guatemalan boat, it appeared to be a fishing boat, however when they boarded it they found that they were actually drug smugglers. They followed procedure, brought the crew on board the cutter. The crew, though, had with them a young dog. Now, since the procedure is to clear the boat and sink it there's just no humane way to leave a dog on board. If they didn't sink the boat the dog would starve, if they sunk the boat they knew they were sending him to his death Shortly thereafter though, apparently within a period of days the dog started nipping the crew members. Crew and the detainees together tried to restrain and muzzle the dog, but by that point the dog was provoked and it bit twenty persons, crew and detainees.

Of course the rabies vaccination status of the dog was unknown. Apparently very soon after the muzzle attempts the dog died, he

could very well have died from traumatic injuries, we have no way of knowing. It would have died of many causes. At that point they threw the dog carcass overboard, the medic was not informed, was not involved at this time of the process so we were left with an immediate question, is rabies prophylaxis needed which is a difficult question in a way because of time and expense as you can imagine.

But preventive medicine opted to go with the yes route. Even though the bits were provoked the unknown status of the dog left us to be immediately cautious. So immune globulin vaccine were procured and were administered as quickly as possible. All the Coast Guard men, of course, complied with the vaccinations. Apparently all the detainees refused their shots. They were taken out by law enforcement, so we don't really have any followup on the detainees.

As you can imagine this lead to

some lessons for us to consider. Should dogs or animals be taken aboard in the first place. Is this an isolated incident, hardly. When various ships are stopped there will be dogs, there will be parrots, there will be all kinds of things that no one really wants to kill.

In fact, coincidentally this is the last issue of the Coast Guard Magazine, the title is Doggone Drug Bust and it's almost the identical story except no bites and no rabies prophylaxis. This happened last November. And, I'll read it really quickly.

"It was great to have a four-legged companion on board, definitely boosted troop morale and we made him a little outcove for sleeping in the hangar if he could just hang out with us. He would sit there when we would do our work and would jump up and down with our jumping jacks." This dog ended up being adopted by the Coast Guard.

So, the next step in terms of

thinking this through is we really have no policy for animals and livestock on board our cutters. Should we have a designated person on every ship trained, to be knowledgeable about restraining of these animals of unknown origin. And, certainly they should know that if the animal were to die that the carcass needs to be saved and housed so it can be appropriately tested.

We were also quite concerned about the report got to us some time after the event. And, there was clearly a delay in terms of potential exposure, of course.

That concludes the update to you and I'll be glad to take any comments or criticism.

PRESIDENT OSTROFF: What a fascinating story. I would never have imagined, but it makes perfect sense, you know.

CAPTAIN OBRAMS: We thought we'd share this with you.

COLONEL GIBSON: Do you have in the policies that you're developing, have you considered cages and most of the rabies are dogs, cats, et cetera. And, they can be at least caged.

CAPTAIN OBRAMS: They are. And certainly our cutters are large enough that we can have an area to keep restraining cages on board, yes.

DR. ZAMORSKI: I'm wondering what your policy is with respect to rabies immunization before people deploy?

In other words, are those people who are likely to get pets or animals, are they typically rabies immunized?

CAPTAIN OBRAMS: No. It's hard to define which areas are the ones that people would be at higher risk, you know, you never really know when you're going to come across an interdiction process. Guatemala isn't necessarily a high risk area for rabies so it

would be a very difficult policy...

COL. GAYDOES: I would strongly recommend the animal control or training, because some of the worst incidents I was involved in when I was in the U.S. Military came about because people were not properly trained capture and restrain animals.

Another thing that we have a lot of problems with is how to euthanize the animal.

It was not uncommon for us to get the head of a very small animal that has been euthanized, but a rather large powerful weapon.

CAPTAIN OBRAMS: The medics, for example, could euthanize them.

DR. KILPATRICK: This was a very interesting story, but could I get back to the last presentation. We have some 30 to 40,000 deaths per year from rabies in the world. And 95% of them are South Asia, India and Pakistan. So given where a lot of the other soldiers are what is it that we are doing for prevention and

prophylaxis in Iraq and Afghanistan and Pakistan?

COLONEL UNDERWOOD: We do not routinely, we don't give prophylaxis with rabies vaccine to our troops going into those areas. We do put out information to stay away from dogs and animals. What is of interest though, I think, this was several years ago, there was a human case of rabies, it was discovered in the states with a child who had traveled through India and was feeding the monkeys. I don't know if you remembered that, it was like six or seven years ago.

So more recently we had a group that was going TDY to India and were stationed in Alaska and we put out information, "do not feed the monkeys in India, whatever you do." That's something people think about dogs usually but not harmless cute little monkeys, But no, we don't routinely do it.

PRESIDENT OSTROFF: And, I'll

point out another rabies hot spot is Haiti. We have had a number of cases in the United States that have come to the United States because that were not vaccinated.

COL. HOKE: There are troops sent out routinely immunized against rabies, many of our special forces operators aren't.

PRESIDENT OSTROFF: It does strike me that there are probably and I'm sure you've been thinking about how they to generate policy around proper handling of animals that might come aboard your ships, and I think some of the issues that you raised are very good issues. Particularly around how the animals are housed and held. And, having a designated individual aboard each cutter whose responsibility is to properly look after those animals it seems to me that now that you've seen that this is a problem that you're probably going to have to have a policy.

Our next presentation is from our

colleagues across the water Great Britain and we have Colonel White and it's very good to see you. He's a medical liaison officer.

COLONEL WHITE: Thank you very much for inviting me for the UK update.

This is from a UK newspaper not so long ago. It was a 2002 and a part of 2003 and a report was provided to (inaudible) last year.

(inaudible) share some of those thoughts with you today.

The report is a hundred and sixty pages long and forgive me if I run through the finances part rather rapidly instead of reading every line to you.

I'm going to pick up here you're not going to see programs related to deployment for a number of reasons. One is for the average British soldier deployment, we have a six months rotation policy for deployment. (inaudible) and the time to react to our problems is limited.

And on the final bullet, they are

actually quotations but I suppose it might be (inaudible)

The problems identified were actually discussed with a medical practitioners.

(inaudible)

These are the conclusions of the shorter questionnaire and on both questionnaire it contains personal and deployment related questions and I've provided both of the questionnaires. This is just a very simplified (inaudible) of the study design by -- criteria for the medical practitioner which are based on symptoms, general health questionnaire, PTSD and (inaudible) out of states and (inaudible). In order to investigate the validity, an equal number of people also identified as having a health problem were referred to a medical practitioner. A lot of the study was conducted were told very briefly discussed later on and then the pilot study was always a possible feature event and the study was designed so that

the study would be used later on.

This is just a note that there were a few other questionnaire included in the study.

(inaudible) 67% was deemed to be satisfactory by the investigators although three mailings were tried to achieve it. And it was comparable with other military service.

On the second bullet there the percent refers to both cases and non-cases and 50% of those that did not attend did respond to a questionnaire asking why they didn't respond and most common reasons were to do with not being able to get the time off. And this study also overlapped the beginning of deployment to Iraq.

But a significant number said something along the lines of what is the point, nothing will be done. (inaudible)

Referring for a minute to the pilot study 73 questionnaires in the pilot study

said they would be in favor of a (inaudible) although there are many reservations. The procedure was that they continue their questionnaire and then they were immediately interviewed 15 to 30 minutes later. (inaudible)

I will read some of the quotations from the interviews. Under lack of trust in the military, " ...medical in the military can't be trusted and they're rubbish." Another one said, ... "American tanks (inaudible) uranium. I think there is a MOD conspiracy to deny any problems and the doctors are all part of this conspiracy." (inaudible) "I would only insult a doctor off base, this is a medical assist talking, especially after I have a drink."

Another one said, "I have not answered honestly as deployment prospects would be affected."

No. 4, "qualifications of military medical personnel are terrible."

(inaudible)

Thank you very much. I will try to answer any questions but it is not my data but I'll try.

PRESIDENT OSTROFF: Thanks very much. Let me open it up to any questions or comments. I just have one quick one, where did they come up with ten minutes and 24 seconds, ten minutes and 24 seconds that they had to be able to run 1.5 miles.

COL. WHITE: Did it say that? But that is one (inaudible)

(LAUGHTER)

PRESIDENT OSTROFF: I mean, is that the standard?

COL. WHITE: I should say that usually fitness in the Army includes a component of upper body strength exercise but it also included for many many years a one and a half mile run.

PRESIDENT OSTROFF: Dr. Shamoo.

DR. SHAMOO: Thanks, Shamoo. Is

the (inaudible) is that based on biochemical data on a human being for four weeks or six weeks or eight weeks?

COL. WHITE: I asked the question, what is this based on, I think it's based on some physiologist doing some tricks in equations that were used in coming up with this. I'm not sure that there is any study done.

DR. SHAMOO: Because biochemical congregation at this time in Europe is well known and it takes quite a bit of time.

DR. PARKINSON: I just wanted to commend you and your colleagues for crisply stating one bullet, the adverse consequences of (inaudible) screening programs. That highlighted blue paragraph, particularity the - - respondency on health care providers, we've all lived through that. So on a personal note thank goodness for a very rational approach to doing a piloted attempt rather than rushing in and saying the more screening the better. I

think for a lot of people on this side of the pond can probably learn a little bit from that. Having said that it leads me to think that maybe we're going down the wrong track with this screening paradigm that we have which is find the people at high risk and fill in the blank, as opposed to saying everybody at equal risk and let's make sure the services are equally available to the whole population to address those needs.

What your study also shows there area lot of needs out there. And how an individual attributes that to their service in or out of Iraq or in or out of sitting on an American tank is something that we all have little control over and we could try to mitigate the best we can miscommunication, but to me at any rate it's not a question as much of just get us thinking here, is there a better approach than multiple serial constant screening oftentimes will little intervention.

Hyperlipaemia programs. Easy to get the screening test, but what are you actually doing to (inaudible) and we go on and on with this paradigm and you just said it very crisply in a way that's very useful, but I think this has (inaudible) should think about going into a huge return to home program that we're going to be having coming out of Iraq.

COL. WHITE: I didn't address any of the quotations in the medical stuff.

DR. ZAMORSKI: Question on screening, I guess I just don't come to the same conclusions, you know, in terms of deciding that well screening isn't valuable because this one particular - - or one particular instrument done on a multi group of people in a particular setting and it suddenly means that screening for mental health problems isn't worthwhile, well, or done this way, isn't worth while absent other things going on at the same time.

But it's clear that there's a huge

burden of untreated mental illness in the general population. It is clear from the primary care setting that screening results in clinical untreated depression if and only if it's associated with implementation of appropriate therapy and symptomatic followup.

COL. WHITE: I think I intended to (inaudible)

DR. ZAMORSKI: Fair enough. The last comment is just that the positive predictive value of 40, whatever percent it was, the positive predictive value of the test for the screening for 43% is extremely still not bad at all.

COL. WHITE: (inaudible)

DR. ZAMORSKI: Well, know, I'm just saying that screening processes are typically an issue.

PRESIDENT OSTROFF: Thanks very much, our certainly last, but not least is from our Canadian colleagues and it's my

understanding that Dr. Zamorski is going to do it.

DR. ZAMORSKI: It's a team effort. So I'll just say a couple of words. Thanks for a brief opportunity. I don't have any slides. This was meant to be sort of a teaser. What I'm going to do is list a few projects that we're involved with currently that will come to some fruition over the next few months or so to sort of have you think about whether there would be things you would want to bring additional people beside me back to talk about and one of them was the (inaudible) study which I've already mentioned.

The other is, just a reminder again, we've completed a huge mental health survey for around 8000 of our members which was done in tandem with a general population mental health survey done by statistics Canada and this is I believe the first thorough and systematic analysis of the mental health of its military in

tandem with the civilian population and this is the data set that's huge, there are probably a thousand variables for each individual and we're looking at risk factors, we're looking at adjusted problems and if there's any increased risk of mental health problems in the military versus non-military and some of the key findings so far and probably the most important one is about double the risk of depression in our military compared with the Canadian general population in age and sex.

The other was a low prevalence of PTSD around 2.8% with problems with PTSD. Of course we (inaudible) of people with PTSD, so it should not be interpreted to mean that the military service doesn't cause PTSD but it does give us some sense of public awareness in the population as a whole and this is one of those studies that is going to be providing interesting sort of findings for a long time to come. So that's one project that might interest

you.

Another is we've got a team go in to try to validate the (inaudible) NATO classification in our rotation in Bosnia. I don't know how familiar you are with the (inaudible) NATO. But it's a NATO diagnostic classification system. It's supposed to be used in deployment setting and there's about thirty EPI NATO codes and the idea is everyone that goes in to a medical treatment facility in theater will have that encounter coded as one of the various EPI NATO categories like injury of the leg or gastrointestinal illness or febrile respiratory illness or something like that. And, the idea is by using this standardized scheme you'd be able to collect data from the multi-national force and interpret, which makes sense in the context of increasingly multi-national presence.

We had concerns that the system may not actually be very valid. And, so a team

went in to try to look at all the EPI NATO codes that were assigned for people on that deployment and compare it to the medical record to try to see if they could yes the codes were assigned properly and if they weren't why not?

Without going into great detail the data were dismal and there was extremely poor ability to code reliably on EPI NATO based on that record and the codes that are trained people to come up with different drastically from those that the medical staffing theater assigned. There's two particular interpretations here, one is the system is flawed, the other is the application was flawed and the Canadians in that particular deployment weren't especially cleaver.

If you actually look at the system it doesn't take too long to figure out that the system is (inaudible,) it does not provide mutually exclusive categories for coding the problems. And, so they've got a category for

infectious disease and a category for GI illness. Well, if you have infectious gastroenteritis where does it go. Now, apparently there's some rules the higherarchery set rules, but to actually find the list of rules and use them is difficult. So that I think was a interesting sort of exercise as well.

We also did validations of -- we do a health and lifestyle information survey which is done on a periodic basis. It's sort of like our national health interview survey in a sense looking at behavior risk factors, helping with the mental health symptom, et cetera. And, we wanted to compare that data to our mental health survey, just to try to ask the question about whether the results of the mail survey of health behaviors and health status could be compared to a much more rigorous interviewer based 80 plus percent response rate that we got through our rigorous mental health survey.

Again, what we found was is that there were important differences between the two that were either accounted for by secular trends, which we don't think is likely the same, because the data didn't come from the same time period, or because of some anonymous bias because the response rate to a mailed out lengthy health questionnaires being different from statics Canada calling you up and say will you participate in this personal interview. And the mode of administration is probably very important.

I spent a fair bit of time comparing without really appreciating this, comparing paper survey results with the national telephone survey results and there's a very systematic difference between them. And, so if you're administering periodic health surveys and you're trying to compare it to standardized general population numbers you have to make sure that your mode of administration is accounted

for.

So it's an interesting piece of work as well. We just completed a linkage study of our Gulf War veterans with a randomized control group of (inaudible) veterans with respect to mortality and cancer incidents. Because we do have a national cancer registry and that data will be available probably early in the summer and finally we started s sick leave data that is to try to track sick leave occurrence over time, and in essence this was just leaked to the media recently so I can share it with you, otherwise I couldn't have which proves that the media sometimes has some value, but our findings in essence were that sick leave is slowly increasing. That there are huge rate variations regional, particular problems in Quebec, for some reason, has approximately three times per capita of sick leave rates as other bases, didn't matter if it was Navy, Air Force base or an Army base. So that was peculiar.

A small fraction of people accounts for a large fraction of total sick leave days, and in our case the number of people who are really on long term sick leave was actually a little number of people, meaning 300 out of 66,000 accounted for what was these really long sick leave people.

That's kind of good news, because it means those are the problem people who are the most disruptive to operations because they're sick and they're not working and you can't get fill the positions because, you know, they are still in it.

Then the other is the substantial contribution of mental health problems, particularly depression of the PTSD secondary to as it cause for sick leave.

So those are just some ideas that you might want to -- you can contact me and I can put you in touch with the person who is actually responsible, thanks.

PRESIDENT OSTROFF: Thanks very much. Let me just ask if there are any questions or comments about the information that was presented.

Thank you very much.

Before we turn the microphone over to Colonel Fensom, I would like to mention that there are two preventive medicine liaison officers who visited us are our last meeting.

As I mentioned one of them was Colonel Woodward from the Air Force, who was unfortunately not able to attend this meeting, but we have thoroughly enjoyed for the last several years his presentation and the input that he's provided and we have a plaque and a coin for him and then lastly Colonel Fensom from Canada who has been with us as certainly as long as I've been interacting with the board and has also been invaluable in terms of her liaison role with our Canadian colleagues to the north and we also have a plaque and a coin for you.

(APPLAUSE)

COL. FENSOM: All good things come to an end and my tour here is coming to an end.

I'd be really remiss I think without expressing my real appreciation to the board for allowing my participation and especially to my (inaudible) colleagues for accepting with open arms a family doctor into their rarified world. It's been truly an education for me.

I tried to work at a (inaudible) between this group and the (inaudible) CFMG and I think the increasing presence of folks coming down from Ottawa to do this is proof that there's been some success and I know that in the future I know there's going to be a lot more for exchange of information and collaboration.

We're going to continue to be long term allies and I think whenever we have a large group of recruits on the ground together in the same place that it's going to be critical, as

always, to avoid reinventing the wheel between ourselves especially on a risk communication basis to develop more and more ways of seeing from the same input (inaudible)

I've been in D.C. since August of 2001 and I know that it's been a trying time for your country. It's been an opportunity for me, though, to see and experience in a very intense way the incredible valuable contribution of all the (inaudible) to the ability of the services to do their jobs. I've seen you offer many silver second thoughts when needed. And, I think perhaps more importantly what's unique in the capabilities of this group is that you're the only ones that can provide that science based independent opinion on issues of medical policy or besieged by political influences and by populous influences and I think that is invaluable to the uniformed personnel that are so dedicated to caring for the soldiers. And they can't get it anywhere else in my view.

I certainly see in this room uniform and civilians, very abundant evidence of a lot of selfless dedication to country and helping the troopers and that's been a continuing inspiration to me.

I think that your accomplishments are self-evident -- some of the lowest (inaudible) rates in history for recent operations. (inaudible)

As I move to Iowa to do my penance and take charge of the medical policy production group at headquarters I'm going to try to see if we can establish or reestablish an equivalent (inaudible) -- we don't have a group like this and in my view I think that we need one.

So I just salute you all and I wish you the best in your continuing endeavors. It's been a real privilege for me to be in your company and best wishes for the future, thank you.

(APPLAUSE)

PRESIDENT OSTROFF: Thank you for your very kind words and we'll certainly miss you and you're welcome back at any time.

Our last presentation of the day is an update on influenza surveillance and we have Major Andrea Krull from the Air Force Institute of Operational Occupational Health in San Antonio.

MAJOR KRULL: Good afternoon. Apparently I lost the coin toss in being last on the agenda. But hopefully it won't be too painful in moving right along on a topic that obviously importance to me and hopefully to the audience.

I'm going to present an overview of the 2003-2004 influenza season from the perspective of the DoD influence surveillance program.

There are several components to this program and this DoD influenza surveillance program is under the auspices of DoD-GEIS,

Global Influenzae Systems. First a comment on the population based recruit surveillance which is managed by the Naval Health Research Center. They have a very targeted program, they are febrile respiratory illness surveillance which is a trainee populations recruits from all services.

And, because they have actual populations they actually track the incident rate of febrile respiratory illnesses and they do this in a very systemized. And, while their program is very focused the worldwide sentinel surveillance program which is managed at Brooks at AFIOH it has much broader implications.

So we have sentinel sites that collect specimens that meet the ILI case select illness definition. I've noticed that this past year we really did focus asking our sentinel sites to submit specimens from those individuals that were vaccine breakthroughs or manifested with server illness.

In addition to getting sentinel specimens we also included clinical specimens. Brooks biology lab or Brooks AFIOH lab is the clinical reference of the Air Force for getting clinical specimens and those are included in the specimen collection.

I have to say that this year we continued to enhance our relationship with CDC who we had an ongoing relationship with and I think that (inaudible) by our recommendation last year to WHF collaborating lab.

Each year we've worked with FDA vaccine and related biological advisory committee in providing input for their annual meeting and in certain cases we've actually provided seed viruses for the vaccines for the following flu season.

We do collect data from the Army, but these specimens are specifically collected for clinical purposes. Even though my talk is not on adeno, we heard a lot of discussion about

that this morning, and this certainly reinforces the importance of moving forward with the adeno vaccine.

As you can see from the panel that adeno continues to be the predominant bio-respiratory packaging that they identify in the recruit population from all these trainee sites.

However, since we are talking about flu, just to comment on the flu specimens that are collected from the Naval Health Research Center, and while these numbers are relatively small it does generally -- the patterns generally do go along with the peak patterns that occur in the nation. This is flu activity over the last couple years.

Turning to the worldwide sentinel surveillance program which is the focus at the top made a few comments about this diagram. In addition to DoD-GEIS, I listed the Air Force SG's office at the top, it's because the Air

Force is the effective agent for this program. And, there's two organizations within AFIOH the of course Institute for Operational Health and we work very closely together. We have the biology lab and then the EPI services branch which is where I'm located. And we work very closely together in collecting both specimens and information and transmitting that information.

The overall purpose of this program is to No. 1, identify circulating the strains. Two, to determine if there's any variant strain and No. 3, ultimately to determine or to assist in determining what the vaccine strain is for the following year. We have increased our interactions on the EPI side of CBC, there's always been ongoing interactions with the lab site so we definitely can start collaboration on the EPI side of the house.

This is a map that identifies the locations of our sentinel sites throughout the

DoD system worldwide and I would just like to make a few comments and No. 1, we have several conditions that are met or need to be met in order to be selected as a sentinel site and those conditions include the location, the second being remission and the third is really an interesting part participation. So as you can see we have a fair number of clustering in the Asian Pacific region. We also have ports of entry in the United States and then as you can see in the central part are actually all the trainee locations.

Now, I'd like to comment on the last line which talks about new sentinel sites. And, as you can see we have a few sites on the West Coast for those Navy locations. We actually have a Coast Guard location in Alaska. We have an Air Force location in Italy and of note and of interest to many people are the two locations, one in Cutter and one in Ketchikan near deployed locations and we've put a lot of

interest in getting specimens from those locations.

One last comment to make on this particular slide are the crosses and they are the DoD overseas research labs and we always had a relatively good relationship with them in South America, but this past year I think that we have re-engaged with two critical locations in Napal and Thailand and they are becoming very very beneficial.

This particular graph is actually the number of sections submitted to Brooks to the biology lab this past season and as you can see the peek activity is weeks 49 to 51 and that corresponds with the height of the flu season for this past year.

One comment to make about the volume, as you can see we're approaching almost 400 specimens in one week. The lab can handled approximately 300 specimens per week or 60 per day efficiently and effectively. But once they

go over that amount it becomes quite difficult for them to handle. This actually works in a way as a good exercise, practice that is for a epidemic event or a bio terrorist event in that they had to implement their search plan and they have both an internal and an external search plan to handle such increase in volume and part of that includes sending specimens to (inaudible) in San Diego.

(inaudible) as I think everyone knows this is clearly the flu season. And, in fact, approximately 30% of all the specimens received were positive for flu and that's quite high and that compares to about 20% of specimens received from the CBC.

And, of course we know that not only was it a flu A season of approximately 99%, but that it was on exclusiving 3 and 2 season and specifically the that the parian flu strain. So very traumatic H3N2 season and more specifically the (inaudible) strain. So, very

traumatic H3N2 season with very little activity in HNI1 or even with these (inaudible)

One region of the world that, of course, particularly in Asia/Pacific area because so many strains come out of this region. So a couple of comments made on this slide. No. 1, specifically the earliest specimen -- that we get that are positive for flu come out of this region and this year was no exception.

All these new specimens, all the specimens that came in October that were positive for flu came out of this region and in particular from the upper states in Guam we received the most positive this year.

A different perspective is the breakout of specimens from the sentinel sites and non-sentinel sites as well as the overseas lab, and again to comment on the importance of the role of the overseas lab, a relatively goodly portion coming from our overseas labs partners.

And, then just to comment on the adeno and why it's so high on the non-sentinel side, that is because of Lackland Air Force Base, which of course the recruit, the only Air Force recruit center currently participates within the Navy (inaudible) program and approximately 70% of the adeno that need collected or specimens that were positive for adeno came from Lackland this past year.

Turning now from actual flu specimens, talking about some of the surveillance data I'd like to comment first on essence. Essence is a DoD GEIS product that -- for surveillance and as you can see identified the number of categories, we have seven categories, and one of those categories is respiratory which is a very large group ... In place DoD-GEIS was shortly after 9/11. However, in October of '02 a subset of respiratory category was identified that more closely -- is more closely associated with those symptoms and

associated with influenza illness.

So since October of '02, which of course is reporting is in October, we have this data that comes from DoD medical treatment facilities worldwide and this is an ongoing listing update that represents influenza like illness surveillance.

Now, what we have done with this same data is refined it to get a more complete picture than what you can see in this graph that was produced from our office is it gives you several layers of information. You can see the same data as you saw in the previous slide.

So in this case we, of course, have the current year activity. We also overlay it with last year's activities. We have the inter-seasonal baseline that is week one which is the first week of May, so we know what our theater seasonable baseline is. And, then you have (inaudible) line so from the same data source we can provide a little additional

information in terms of not only the current activity but the (inaudible) of that activity for the entire DoD military health care system and then specifically for the sentinel location.

This information is available under AFI website and it's also sent out as part of the weekly report that goes to all the sentinel sites, and various interested parties throughout DoD.

Another recent addition to the mapping and to the various options that we have available on the AFIOH website is this map.

Now, what this does not do is indicate the severity of illness for flu activity, it's strictly relates to the number of specimens. Now, of course, we do not have sites in every state, so we do have concentrations, but again it just provides additional information and narrows it down to a specific base and find out where that activity is. But again that's not associated with severity, it

just indicates where the specimen had come from.

While clearly influenza is of course the basis for this entire global surveillance program. It's also become a foundation for accessing and monitoring activity that can be associated with any number of nationally occurring bio terrorist agents and certainly more recently with SARS and Avian flu, and so use the foundation and the data sources that we look at and then use it and then colporate it all together, so it's really broadened in its implications and not just the flu activity.

There's always been an interest in vaccine breakthroughs and so in the last few years on an ongoing basis we've been collecting that information.

Now, as you recall at the beginning of the briefing I mentioned that specifically as to sentinel study to submit specimens on vaccine breakthroughs as well as

CBC's, so we use the Air Force tracking system as well as the lab data using the definition of data vaccination being greater than 14 days prior to the specimen collection. And, that then revealed approximately a 22% breakthrough. But that is strictly observation. It certainly isn't scientific because it's just -- there's nothing standardized or formalized about that. But it's strictly an observation.

But what it stresses is the importance and also the interest in doing more defined vaccine effectiveness study.

In this past year each service made some attempt to define vaccine effectiveness. Now, the methods and results very significantly, but I want to at least mention that the attempts that were made by each of the services to at least address the issue of vaccine effectiveness. I'll start with the Navy and Army and finish with the Air Force.

So commenting on the Navy. The

Navy used their existing tried surveillance... from December, you recall that's the (inaudible) activity for this past year. And, they selected trainees or used data from trainees (inaudible) recruits locations. Now, this is all based on culture positive results.

This was done by mathematical modeling, specifically person, time, analysis and and they looked at (inaudible) that list and vaccinated...

Now, just to give you an idea of numbers, these numbers actually represent -- the numbers were generally small, but these were from all eight basic training or basic recruit locations in terms of culture positive results, for influenza and then just a very (inaudible) that were already vaccinated.

So in the case of NHRC what the end result shows they ended up with four models and that was based on the fact that they had four sets of assumptions. And, the reason they

had four sets of assumptions was because each services recruit training process is somewhat different. It varies length of time for each of the services and they vaccinated at different points, so they relatively -- this is their best and worst case scenario.

Having said that you can see that their effectiveness was extremely high going from a low of 87 to a high of 94.

Now, given that we said on a good year where there's a good match 70, 80% is considered good for effectiveness and this is incredibly high in terms of the effectiveness.

Now, the question is whether it's generalized or not, of course, would be different.

The next study that I'd like to comment on would be the Army. Basically what happened with the Army they had an outbreak in trainee populations at Fort Lee and so the folks there requested a CHPPM to send an EPI

consultant team down to characterize the outbreak, and we had a representative from AFIOH as well that participated. So in the course of characterizing this outbreak they made an attempt to determine vaccine effectiveness.

The problem was it became very difficult to clearly separate the cohorts in terms of the exposed and non-exposed.

And, there were a number of other impounding factors and interactions so ultimately the confidence limits were extremely wide and the bottom line was they didn't feel that the rate of conclusion (inaudible)

And, then turning to the Air Force study which I of course have the most information on. What we attempted to do at the AFI was the secondary cohort study and we tried to identify from index cases and all the index cases were culture pods so that was a start, but the focus starting with the index cases we tend to look at secondary family contact. And this

was the cohort for the studies.

Now, we collected data from all the family members. And this was done by telephone survey and in the process of this survey we collected the vaccine history, the date of onset of symptoms and then attempted to characterize the symptoms to make sure that they met the case definition of IOI. And, that was all self reporting information.

And, then finally based on that information we attempted to calculate the secondary attack rate comparing those vaccinated versus unvaccinated. And, here's the data that we had on that study.

Now, we start by saying there were 414 eligible. What that means is that that includes all the index cases that we had plus family members. So in other words if there were no family members then we went through the various demographic and all the data sources to determine if there were family members, if there

were no family members they were excluded, because to be eligible they had to have at least one family member. And, so between index cases and family members that gave us a total of 414 eligible.

Ultimately we gathered data from 243 individuals again, again a breakout of those index cases and household contacts. A relatively high percent received the vaccine on household contents. Now, keep in mind that a large percentage of that could have been the active duty member. Ultimately our goal was to determine a secondary attack rate and in this case the vaccinated group had a 23% attack rate versus 38% of the unvaccinated leaving us with an unadjusted vaccine effectiveness rate of 39%.

Now, our plans for the future for this is, No. 1, to repeat this approach prospectively for next flu season, but to do this on an ongoing process so that we reduce any recall (inaudible) data from this past study,

the data was collected in November and December and some interviews occurred in January so there could have been up to two month delay between symptoms and being interviewed.

We want to include more active case finding using a variety of data sources. But again still going with the agent, but you have to start with culture positive results as our index cases.

Now, one component that was not included in this past season is to validate the data with medical records, vaccine registry, and that implies that this was an exempt protocol so we were not able to look at the data for this year's study. And, again we hope to continue looking at the secondary attack rate using that as our estimated for vaccinate trafficking.

Now, at this point there is a draft code protocol, but the plan is to discuss the protocol at the upcoming DoD influenza working group meeting and then once it's

discussed and protocol is finalized then it would be submitted for IRB and Air Force approval.

So the activity for this past season it really wasn't an exceptional year in that A and specifically A/H3N2 predominated so dramatically and was specifically that it was the enterovirus (sic) stain in almost all cases. We saw very few Influenze B to day 13 and 50% of the (inaudible) that were self type only two were 2 were H1N1, so just dramatic.

And of course this is very consistent with the CBC data. And as far as any of the adeno, the H5 and H7, we cannot identify any AFIOH.

Of course, the molecular analysis supported and everyone pretty much knew it was the parain (sic) strain in almost every case. vaccine strain.

It also provides us with an opportunity to refine the influenza lab, that is

our search plan. What would we do in the event of an outbreak or bio terrorist event when we will just inundate it with samples.

Additionally we increased surveillance by identifying new surveillance sites, we continue to explore getting specimens from deployed locations we did get positive results from Kyrqyzstan, they are very difficult to maintain because of the logistics and constant turnover, but we continue to pursue these.

Also I should mention our continued collaboration or renewed collaboration with some of the DoD overseas research labs which are really a critical part of this.

We at least made an attempt to perform vaccine effectiveness studies and of course our intent is to refine this process in the coming years.

And finally, I mentioned that there was an upcoming DoD and preventive

surveillance working group and that meeting actually takes place next week in San Diego. This meeting is directed by health affairs policy and as you can see the two participants, of course all DoD representatives are there, but we do also have other federal agencies that will be coming to (inaudible) and of course topics of interest to go over season summary, a lot of what we heard today. The focus on the vaccine effectiveness. There will be a subcommittee that meets to discuss the studies that were done and make attempts to formalize them and put status protocols for the season. To look at the sentinel sites that we currently have at each site and to drop sites, if necessary. And, again to expand interactions of the overseas research laboratories which are a key partner and of course to plan for the next flue season.

That concludes my briefing. I will take any questions.

PRESIDENT OSTROFF: Thank you very

much. That was a very nicely put together and very nicely presented overview of the season and I guess if I could ask one question first you know your data -- the information is wonderful on the basis that you can get virtually any estimate of vaccine effectiveness, depending on how it is that you do the study and, you know, this was a season where this was a big issue and we got results for all over the board too depending on what that mission to use and how you did the study. And, I sort of have become convinced that it's not as important what the exact methodology is as is to try to reproduce it to season to season to season, because it's probably the comparators from one season to the next which is a better, you know, if you are all using the same method, each time it's a better estimate for you of when the vaccine is performing well and when it's not performing well. Then trying to do different types of studies continuously because you can get any

answers that you want. And I get a little bothered when you say you're going to try to continue to refine and refine and refine the methodologies around your effectiveness studies, because you'll just keep on coming up with different answers every year and you won't know whether those different answers are meaningful.

So it might be more prudent to try to settle on one particular method and do it the same way and the same place.

MAJOR KRULL: I think that from the Air Force perspective at least we did not include all the components that we would have liked to in particular because of the IRB issues and so this was kind of a skeleton of what we would hope to do and I think once we have all those components then we can attempt to conduct that (inaudible)

DR. HAYWOOD: In your comment I was intrigued by the low rate and knockdown (inaudible) North Carolina versus California

considering the troop distributions in those two locations. Do you have an explanation for it?

DR. KRULL: Are you referring to the map?

DR. HAYWOOD: Right.

DR. KRULL: Again as I said that map just indicates those specimens that were submitted from those locations. And, again we only had sentinel sites in a variety of locations based on certain criteria.

We don't have any sentinel sites in North Carolina, we have two sentinel sites in California, so again it doesn't represent the severity of illness it just goes (inaudible)

DR. HALPERIN: It was a nice presentation. (inaudible) the worldwide system, I guess the goal is an earlier identification of flu than (inaudible) can provide. Does your system identify...

MAJOR KRULL: You mean, in terms of the actual surveillance data...

DR. HALPERIN: The detection of the epidemic does the worldwide system detect it earlier than what the (inaudible) otherwise if that's not the goal then I was just wondering what the goal is.

MAJOR KRULL: Well, there's several parts of it and again, as I mentioned, is that No. 1, to identify what's circulating, any variance to that. And, again part of what we can offer DoD is to provide sites in one case or in some cases to access locations that other systems don't have access to.

And, again at that point specific locations tend to be of such high interest because so many strains came out of that location.

We have a lot of DoD military installations and then again with our renewed interaction and development with our DoD overseas labs and particularly Napal and Thailand, they provide us with an opportunity to

collect specimens that no one else may have access to. Dr. Gaydos, it looks like he's ready to comment.

DR. GAYDOS: Yeah, the only thing I'll comment on, I mean this system has been fabulously invaluable and with that said, getting specimens from locations that otherwise are relatively inaccessible and picking up new variants in the system over especially in recent years has provided the strains that (inaudible) vaccine because they find them first.

DR. GAYDOS: I think there are three things that we looked at when we looked at our collection sites.

One was to identify sites that we could collect at that where other organizations couldn't. And, collection sites are coordinated every year with the CBC as Andrea pointed out, some of these sites the Department of Defense is the only collecting organization out there.

The other two things we looked at

the training site of the United States, because these are unique organizations where we bring in young people from across the country. Actually from (inaudible)and they are in close quarters and we don't know what's going to happen there.

And, the third thing is that the sites that you see in the United States and overseas in the military sites those sites represent populations that are highly mobile and so, for example, we have air crews that are operating out of Germany where other people may be collecting, but our air crews are traveling throughout Asia and down into Africa, but for those reasons we think our populations are a little different in those collection sites.

DR. HALPRIEN: On your slide 9 where you had your Asia/Pacific specimens. If I interpreted your colors correctly about 25% or 30% of your weeks about 48/52 had no virus specimens in there? Were those adenovirus outbreaks in deployed forces?

MAJOR KRULL: Well, actually typically adeno of course is concentrated not only with the recruit populations but in trainees but this year we actually had 22 specimens from our two Air Force bases in Japan and it's higher certainly than we typically get so when we checked with the basis they were -- they couldn't classify them or characterize them into a certain population, trainee populations, but it clearly got our attention, because that's a relatively high number of adeno and again 22 that was the largest concentration outside of any training location.

MEMBER: One of our concerns with the current situation is that since we're not giving the vaccines, that the people who pass through the training sites during the inter epidemics periods may in fact (inaudible) if we have enough of them we could have an epidemic.

PRESIDENT OSTROFF: Last question over here.

DR. PARKINSON: This Avian flu thing (inaudible) I was wondering, the question's a little premature because you haven't had your conference yet, but what types of things are you thinking you might do a little different from this flu season, what's the potential for that particular strain particularly in the Far East.

MAJOR KRULL: We've been trying to be particular to focus in part on our laboratory capabilities including increasing our molecular capabilities and developing new (inaudible) so that we can more easily and more readily detect those strains should they enter into our system.

However, we are primarily falling back, at this point, on the same guidance with SARS in terms of identifying locations. So if we receive (inaudible) location that would be a little different because again we are relying on past history, et cetera like everyone else is.

But we are attempting to at least

be able to identify those factors if they were to come in and we have a very good turnover, but again there's still that first group and any outbreak has the potential to cause problems if it's not identified.

PRESIDENT OSTROFF: Thank you very much. That was a wonderful presentation. That actually ends the formal program.

Thank you very much and I'll bang the gavel, meeting is over.

(Whereupon, at 5:25 p.m. the meeting was concluded)

CERTIFICATION OF COURT REPORTER

I, Donna Kay Evans, the court reporter before whom the foregoing meeting was taken, do hereby certify that the testimony appearing in the foregoing was transcribed from stenographic notes and cassette tape and that said is a true record of the testimony given to the best of my ability.

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Donna Evans